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PHARMACEUTICAL EXPORT AMENDMENTS OF 1986

DECEMBER 18 (legislative day, DECEMBER 16), 1985.—Ordered to be printed

Mr. HATCH, from the Committee on Labor and Human Resources, submitted the following

REPORT

together with

MINORITY VIEWS

[To accompany S. 1848]

The Committee on Labor and Human Resources, to which was referred the bill (S. 1848) to amend the Federal Food, Drug and Cosmetic Act to establish conditions for the export of drugs, having considered the same, reports favorably thereon with an amendment and recommends that the bill as amended do pass.

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I. SUMMARY

S. 1848 as reported from Committee permits the export of new drugs and new animal drugs and biologicals[1] manufactured in the United States which cannot currently be exported because they have not yet been approved by the Secretary of Health and Human Services or the Secretary of Agriculture, as the case may be. The legislation does not affect those portions of the law which currently permit the export of unapproved pre-1938 drugs, unapproved antibiotics, unapproved new drugs and biologicals for investigational use, and intermediates.

Under the bill, drugs covered by the amendments may only be exported to certain countries and under certain conditions. The drugs may be shipped to three categories or tiers of countries:

1. Developed countries with sophisticated drug approval systems comparable to that of the Food and Drug Administration.

2. Other developed countries with an adequate health authority to assure that labeling information is consistent with labeling of the drug approved by a first tier nation, and capable of detecting and recording serious safety problems and of taking appropriate action thereon, and which have procedures and personnel sufficient to administer and enforce the policies of that authority.

3. Countries not listed in number one or number two if the Secretary determines that shipment of the drug is justified to treat a disease or condition in the importing country which does not exist to a significant extent in the United States.

The Secretary is required to establish lists of the countries described in subparagraphs one and two above. The legislation identifies the following countries for inclusion on the first tier list unless the Secretary determines otherwise: Australia, Austria, Belgium, Canada, Denmark, Federal Republic of Germany, Finland, France, Japan, Netherlands, New Zealand, Norway, Sweden, Switzerland, and the United Kingdom.

An unapproved new drug, new animal drug, or biological may be shipped under these amendments only if it meets the following conditions:

1. The drug is manufactured, processed, packaged and held in conformity with current good manufacturing practice and is not adulterated under subsection (a)(1), (a)(2)(A), (a)(3), (c), or (d) of Section 501 of the Federal Food, Drug and Comestic Act.

2. The drug accords to the specifications of the foreign purchaser.

3. Sale of the drug is not in conflict with the law of the importing country.

4. The drug is labeled on the outside of the shipping package that it is intended for export and that it may be sold or offered for sale only in an enumerated list of authorized countries.

5. The drug is not sold or offered for sale in the United States.

6. Approval of the drug has not been denied, suspended, or withdrawn in a final action by the United States.

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[1] For the sake of brevity, the term "biologicals" is often omitted in this Report from the serial listing of the types of pharmaceuticals subject to the amendments. It should be understood to be generally included in the other terms unless the context indicates otherwise.

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7. Manufacture of the drug in the United States has not been determined to be contrary to the public health and safety in the United States.

8. In the case of a drug to be shipped to a second or third tier country, the drug is the subject of an exemption for investigational use, an application for approval or licensing, or a master file containing the safety information required for an investigational use exemption.

9. In the case of a drug to be shipped to a second tier country, the drug has been approved by a country on the first tier list, and the labeling of the drug is consistent with the labeling approved by a country on that list. Further, the labeling must be in an appropriate language for the importing country, and the drug's approval must not have been denied or withdrawn by a first tier country.

10. In the case of a third tier country, the Secretary must affirmatively determine that, on the basis of scientific evidence including clinical investigations, the shipment of the drug to such country is justified to promote the public health in such country because of diseases (such as tropical diseases) or particular health conditions in such country which do not exist to a significant extent in the United States.

11. Notification is given to the Secretary of the initial shipment. Among other requirements, the notice must be published in the Federal Register, and must include an agreement from the importer of the drug that the importer will not ship the drug to a country not authorized under the amendments.

Authority is given to the appropriate Secretary to prohibit shipment of the drug if it does not comply with the requirements of the amendments. Overriding authority is granted to the appropriate Secretary to block an otherwise authorized shipment if it is determined that the drug presents an imminent hazard to the public health in the country to which it is being shipped. In the event that the importer of drugs under these amendments ships them to an unauthorized country, and such shipment presents an imminent hazard to public health in that country, the Secretary is directed to prohibit immediately further shipment to the importer. The appropriate Secretary is also empowered to require exporters to investigate credible reports of shipment to unauthorized countries, and to prohibit shipment to any importer which is breaching its agreement not to ship to unauthorized countries.

The criminal and civil remedies of the Act are applicable for failure to comply with the amendments and are explicitly referenced as available for use against any exporter continuing to ship a product posing an imminent hazard to a prohibited importer or continuing to ship a drug to an importer, knowing that the importer is continuing to ship to a country to which shipment is not authorized.

The bill also calls for two studies. The first, to be conducted by the Comptroller General, will assess the extent and impact of the unauthorized transshipment of drugs, and the degree of conformance with the labeling requirements of these amendments. The second, to be conducted by the National Academy of Sciences for the Department of Health and Human Services, will examine the economic and international health effects of the amendments.

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The bill also makes explicit that drugs for so-called "tropical diseases" qualify for development assistance and marketing protection under the Orphan Drug Act.

S. 1848 as reported also includes an unrelated amendment permitting the interstate shipment of confections containing alcohol to states in which the sale of such confections is lawful.

Finally, the bill specifies that it authorizes the appropriation of no funds for fiscal year 1986.

II. Background and Need for Legislation

S. 1848 as reported from Committee is designed to correct an anomaly in current law, which prohibits United States manufacturers from shipping important pharmaceutical products from this country for export, prior to their approval for marketing by the appropriate United States regulatory agency, to countries which have approved the products. Under current law, three separate statutes are involved in the regulation and approval of these products in the United States. Drugs for human and animal use are regulated under the Federal Food, Drug and Comestic Act of 1938 (FFDCA), 21 U.S.C. 321 et seq. Human biological products are regulated under the Public Health Service Act, 42 U.S.C. 262. Animal biological products that move in interstate commerce are regulated under the act of Congress of March 4, 1913, known as the Virus, Serum, and Toxin Act, 21 U.S.C. 151, et seq. The Food, Drug and Comestic Act and Public Health Service Act are administered by the Secretary of Health and Human Services, who has delegated that authority generally to the Food and Drug Administration. The Virus, Serum and Toxin Act is administered by the Secretary of Agriculture.

The current treatment of new drugs and new animal drugs flows from the 1938 reenactment of the Food, Drug and Comestic Act, at which time the categories of "new drug" and "new animal drug" were created. The reenactment carried over the key provisions now in Section 801(d)(1) of the Food, Drug and Comestic Act, which authorizes the shipment of unapproved substances under the act if they meet a specified set of conditions, including that marketing of the substance be legal in the importing country. While 801(d)(1) contains a reference to "drugs", no mention of post-1938 "new drugs" or "new animal drugs" appears, with the result that only the export of unapproved new drugs and unapproved new animal drugs is prohibited currently.

Thus, the ban now covering new drugs and new animal drugs is not reflected in the policy governing the other products subject to the Food, Drug and Comestic Act.

The Committee notes that legislative history is lacking on the omission of coverage for "new drugs" and "new animal drugs" under section 801(d)'s export provisions. It does not agree that the inference to be drawn is that Congress at the time intended to purposefully exclude new drugs from that section's authority. But while the Committee feels the history of this provision to be of interest, it does not deem it conclusive of the issues raised by S. 1848 today. S. 1848 stands on its own as a significant improvement over the law as currently interpreted and enforced.

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The current ban on the export of unapproved pharmaceuticals imposes hardships on our pharmaceutical industry and our domestic economy without public health benefits, at a time of increasing worldwide competition.

No other nation imposes an export ban similar to that of the United States. Therefore, the restriction creates strong incentives for U.S. manufacturers who are able to do so to move their operations abroad, where they are able to export their products without restrictions. There are legitimate reasons why manufacturers would make such a move. For example, because the Food and Drug Administration often takes longer than foreign agencies to approve drugs, or because the foreign process may be initiated earleir, a foreign approval may be received years before final Food and Drug Administration action is expected. In a 1980 study, the General Accounting Office (GAO) reviewed the approval times for fourteen important new drugs. The GAO found that thirteen of the fourteen drugs were approved in at least one of five foreign countries before they were approved by the FDA. More recent figures show that seventy percent of drugs approved in this country in recent years were approved first in a foreign country.

Thus the manufacturer is faced with the decision either to forgo production until Food and Drug Administration approval is received, thus yielding the foreign market to competitors, many of whom are not bound by local law to observe U.S. patent restrictions, or to locate its plant overseas and begin supplying the foreign market. Ironically, in many cases in which the plant is located overseas, that plant has sufficient capacity to serve the needs of United States market as well. As a result, even after the Food and Drug Administration approves the pharmaceutical, the domestic market still may be supplied by importing the medicine produced by a domestic manufacturer abroad.

While the prohibition on the export of yet-to-be approved drugs has adverse effects for all of the pharmaceutical industry, it is useful to examine how it affects a critical component of that industry—the biotechnology companies.

These companies have enormous potential for the development of new drugs, and for the innovative production of existing drugs. U.S. scientists are responsible for the seminal breakthroughs in this field, and within the last decade many innovative companies have been formed to develop products produced through this research. It is in the national interest that our domestic industry maintains it leadership position in biotechnology as we move from the research to the product deveopment stage.

As is the case for the pharmaceutical industry generally, approvals for the new genetically engineered drugs are being granted in foreign countries, in most cases well in advance of FDA approval. Because the biotechnology companies are generally small, they may have to enter into foreign licensing agreements which call upon their foreign partners to take these drugs through foreign approval processes and market them abroad. Under the terms of these agreements, when a foreign approval is granted, the U.S. firm must either supply its foreign partner with commerical quantities of the drug from its own production facility so that the latter can begin marketing under the foreign approval, or it must trans-

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fer its technology to the foreign partner to enable it to produce its own commerical quantities. Under current law, of course, the biotechnology companies are unable to ship commerical quantities of these drugs to their foreign partners until final FDA approval is obtained. Unfortunateloy, the biotechnology companies may not possess the financial resources which allow them to set up multiple production facilities and thus produce the unapproved drugs abroad at their own foreign manufacturing plants. Thus, these companies are faced with the export of extremely valuable technology. A certain amount of transfer has already taken place, and absent some relief, our domestic innovators will stand by and witness the evaporation of their lead in this crucial field.[1]

Thus the effect of current policy is to drive overseas capital investment and jobs which should remain on our shores, and to widen our unacceptable trade deficit by reducing exports and, in some cases, increasing imports. Moreover, in some cases, the policy compels the transfer of technology overseas.

At the same time, international competition in the development of pharmaceuticals is on the rise, and if current trends continue, the U.S. industry's position as world leader will become evermore tenuous. As shown in the accompanying table, between 1960 and 1980, the last year for which we have accurate data, there has been a marked downward trend in the U.S. share for key indicators: world pharmaceutical exports, and pharmaceutical production located in the United States.

[1] Office of Technology Assessment, "Commerical Biotechnology: An International Analysis," January, 1984, p. 364; President's Commission on Industrial Competitiveness, "Global Competition: The New Reality," 1985, vol. II, p. 281, Testimony of Robert Swanson, and Tim Hart before the Committee on June 5, 1985.

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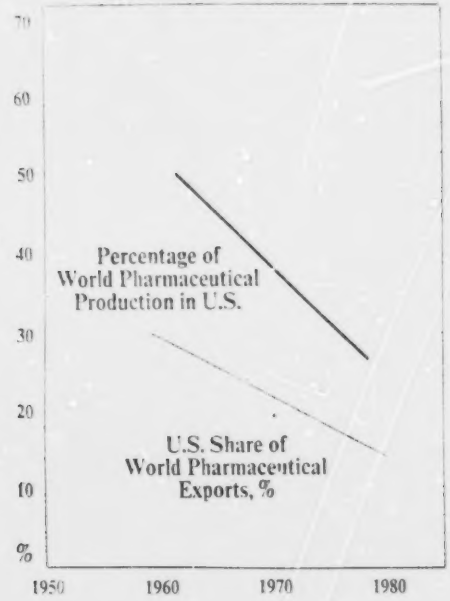
Tenuous Position of U.S. Pharmaceutical Leadership



*1980 - Latest Data Available

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The next table highlights the deterioration in the balance of trade situation. Imports have increased sharply over the last two years, highlighting a five year trend, while increases in exports have begun to level off, yielding a clear decline in net exports. Clearly, forcing our own production overseas only contributes to this problem.

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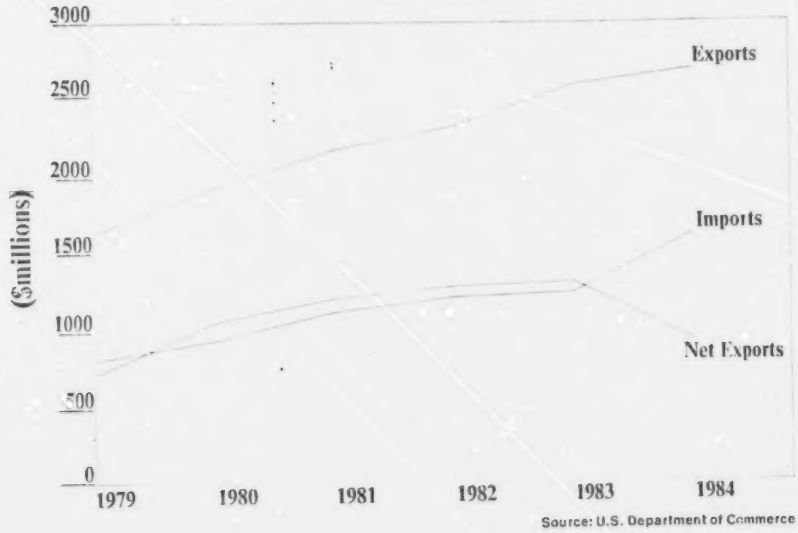
Foreign Trade of the United States in Medicinals and Pharmaceutical Preparations, 1979-1984



Source: U.S. Department of Commerce

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The legislation adopted by the Committee, S. 1848, is expected to provide considerable relief from the sliding balance of trade in the pharmaceutical industry. While future projections are necessarily tentative, they do indicate the magnitude of the improvement which will result if these admendments are enacted. The Committee has considered three sets of figures assessing the impact of the amendments after allowing them five years to reach full impact. An admittedly high estimate of the "maximum potential impact" indicated a $1.76 billion annual increase in exports and the creation of 40,000 new jobs annually. Another study, by Richard Miller, an acknowledged opponent of this legislation, yielded figures at the low end of the scale: $217 million in annual exports and 2,482 jobs. The true impact of drug export reform legislation undoubtedly lies somewhere in the middle.

Using an intermediate, convervative set of figures based on projected export of new drugs not yet approved in the U.S. plus a small sum assuming relocation of a minor amount of existing foreign production, a projection of $400-500 million additional each years seems reasonable. In light of our currently severe balance of payments deficit, this is a very significant figure. It should be noted that it does not include an additional component for a reduction in imports resulting from the statutory change, which would be a reasonable adjustment to the figure. Based on $400-500 million in increased exports, a capital investment of $90-114 millon and the retention of somewhere between 8-12,000 new jobs each year could be expected. Further, there is an enormous potential for the expansion of jobs in the biotechnology field. Genentech, a leading rDNA research firm "estimates that the impact of passage of an export amendment would save from 10,000 to 20,000 jobs in the U.S. biotechnology industry alone over the next 5 years." [2]

Criticism of the differing extimates misses the point—the Committee feels any increase in jobs needlessly forced overseas is unaceptable. By any measure, the impact of drug export reform would be quite positive for our economy and for our domestic labor market.

The Committee is no stanger to legislation intended to revise the current counterproductive law. In recent years, both House and Senate have recommended on different occasions that the obstacles to export be removed. In 1976, the House adopted legislation to authorize the export of unapproved new drugs to any country with an appropriated health agency which has reviewed and approved the drug. It also permitted the export of unapproved new drugs to other countries, upon a determination by the Secretary of Health and Human Services that export would not be contrary to public health and safety.[3] These House provisions were attached to the Medical Devise Amendments of 1976 but were dropped in conference. Subsequently, the Senate included similar legislation as part of the Drug Regulation Reform Act of 1979, which it passed that year. The Senate Committee Report stated, "The provisions of current law which prohibit the export of drugs which are not ap-

[2] Statement of Robert Swanson before the Committee on June 5, 1985, at p. 12.
[3] See House Conference Report No. 94-1090, 94th Congress, 2nd Session, at 65.

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proved for use in the United States should be altered." [4] This bill was never considered by the House.

Easing the burden on domestic manufacturers has also been a concern of the Administration. The President's position was set forth in his Trade Policy Action Plan of September 23, 1985. That plan calls for "allowing U.S. companies to export new drugs and biologicals not yet approved by the Food and Drug Administration to countries where they can be sold lawfully."

At the agency level, reform of the current law has also been advocated by the Food and Drug Administration. In recently revising its regulations to permit the export of unapproved investigational new drugs and biologicals, the FDA addressed as much of the problem as it could without legislative change, and the Committee does not intend that S. 1848 disturb those regulations. The FDA has consistently taken the position that foreign countries must be accorded the opportunity of applying their particular risk/benefit factors to drugs, whether approved in the United States or not. Indeed, the FDA has argued for a less restrictive approach than that set forth in S. 1848.[5]

The S. 1848 approach is also substantially more restrictive than the policy set forth in U.N. General Resolution 37-137, of March 3, 1983.[6]

The Committee feels strongly that the current mistaken policy places needless obstacles in the way of American business, robs our domestic economy of needed capital investment and jobs, and threatens to undercut our lead in recombinant DNA technology, without in any way protecting foreign consumers from exposure to unsafe drugs. S. 1848, as reported from Committee, moves far toward lifting these self-imposed disabilities by authorizing the export to select developed nations of a restricted range of pharmaceuticals which have not yet been approved by the Food and Drug Administration. As will be discussed hereafter, this is accomplished in a manner which safeguards foreign consumers. Indeed, the bill for the first time provides a measure of FDA control and oversight for drugs which are now completely outside of its jurisdiction.

It must be remembered that the current export ban applies only to unapproved drugs manufactured in and shipped from the United States and does not prevent the production and sale abroad of a single pharmaceutical, approved or unapproved, even by U.S. com-

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[4] Rep. No. 96-221, 96th Cong., 1st Session; at 44.

[5] Testimony of Mark Novitch, acting Commissioner of Food and Drugs, before the Committee on June 28, 1984, S. Hrg. 98-1102; and testimony of Dr. Frank Young, Commissioner of Food and Drugs, before the Committee on June 5, 1985.

[6] The Resolution addressed policy on the export of both unapproved and banned materials: "Products that have been banned from domestic consumption and/or sale because they have been judged to endanger health and the environment should be sold abroad by companies, corporations or individuals only when a request for such products is received from an importing country or when the consumption of such products is officially permitted in the importing country." (The Committee notes that domestically banned products would not be exportable at all under S. 1848.)

"All countries that have severely restricted or have not approved the domestic consumption and/or sale of specific products, in particular pharmaceuticals and pesticides, should make available full information on these products with a view to safeguarding the health and environment of the importing country, including clear labeling in a language acceptable to the importing country."

Thus, under the policy endorsed in this resolution, unapproved drugs would be handled under an information sharing system much less stringent than the protections in S. 1848 as reported.

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panies. No case has been brought to the Committee's attention in which a pharmaceutical has been withheld from the world market because of the present U.S. policy. The current ban is completely ineffective for that purpose. Criticism of these amendments on the basis that they might allow some pharmaceuticals to reach undeveloped countries is misguided, since such drugs are now reaching those countries in the absence of the legislation. If produced abroad, these drugs may be shipped to any country without restriction or control. In short, these amendments will have no net negative effect when judged by the ultimate impact on the foreign consumer, which is the only meaningful criterion.

This conclusion is reinforced by the fact that drugs exported under these amendments are a restricted class of drugs which have been evaluated by an agency comparable to our FDA, an agency which has determined that they provide considerable benefit compared to the risk of adverse side effects.

Also, drugs shipped to second and third tier countries must be subject to, in the case of human drugs for example, an investigative new drug exemption or new drug application, or a drug master file containing corresponding safety data. This means that no drug will be exported unless it has first passed animal safety tests which screen out the more severe safety problems. While it is true that most drugs with IND's are never approved by FDA, the Committee does not intend the IND/NDA requirement to serve the final safety screen, as the Additional Views imply. Rather, it is an initial safety requirement which simply augments the requirement of prior approval by a first tier country. It is the first tier country approval which provides the most significant protection for foreign consumers.

In addition, drugs exported under these amendments must be manufactured to exacting standards in conformity with FDA's Good Manufacturing Practices Code, a requirement not imposed on foreign site manufacturers.

This assures high levels of purity, including quality and freedom from contamination. The bill thus protects against the dangerous and unethical practice of dumping inferior products in lesser developed countries. Indeed, export of adulterated or contaminated drugs is illegal under these amendments.

Further, S. 1848 encourages U.S. companies to respond to the often tragic health problems in underdeveloped countries, whose populations are afflicted with diseases and conditions rarely found in the United States. Drugs to treat such problems are seldom submitted for FDA review and approval because it is usually uneconomical for firms to pursue the costly regulatory process where the market is so small.

Thus for many reasons these amendments represent a significant improvement over the current situation for foreign consumers.

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III. Text of Bill as Reported

A BILL To Amend the Federal Food, Drug and Cosmetic Act To Establish Conditions for the Export of Drugs

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled. [That this Act may be cited as the "Pharmaceutical Export Amendments of 1985".

[Sec. 2. (a) The Congress finds that—

[(1) the development and international distribution of safe and effective pharmaceutical products by United States-based firms promotes world health and is important to the national economy;

[(2) the policy governing worldwide distribution of pharmaceutical products manufactured in the United States should promote the public health;

[(3) the full public health benefits that could be afforded by new drugs manufactured in the United States are at times unnecessarily limited by the export restrictions which exist under United States law;

[(4) the current law of the United States does not permit the export of such drugs prior to approval in the United States;

[(5) there are other developed countries which have sophisticated health regulatory authorities which protect the health and safety of their citizens;

[(6) many new drugs developed by United States pharmaceutical companies are approved for marketing in such foreign countries prior to approval in the United States;

[(7) the inability to export such drugs to countries which have adequate regulatory authorities especially hinders the international competitiveness of smaller United States firms and firms in the biotechnology field from entering foreign markets directly, and often such entrance is only possible through technology licensing agreements with foreign competitor manufacturers;

[(8) it is appropriate to permit the export of new drugs to such countries in which they are approved under circumstances that protect against harm to the health or safety of citizens in the importing country;

[(9) the inability to export drugs approved abroad discourages investment in the United States, results in the loss of employment opportunities in this country, and erodes the favorable balance of trade in pharmaceuticals; and

[(10) it is appropriate to provide sufficient safeguards to ensure that drugs so exported are not diverted to countries that may not have adequate drug regulatory authorities.

[(b) The purposes of this Act are—

[(1) to permit the shipment of new drugs prior to approval in the United States only to certain developed countries that meet certain specified regulatory standards;

[(2) to protect against the diversion of such drugs to countries that do not have highly sophisticated health regulatory authorities;

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[(3) to encourage the development and availability of drugs to treat diseases or health conditions which are rare in the United States;

[(4) to encourage new capital investment, the creation of new job opportunities in the United States, and maintain the favorable trade balance in pharmaceuticals; and

[(5) to enable the United States biotechnology industry to enter foreign markets to the extent permitted by foreign law without licensing their technology to foreign firms.

[SEC. 3. Section 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381) is amended by adding at the end thereof the following new subsection:

["(e)(1)(A) A drug (including a biological product) intended for human or animal use which—

["(i) requires approval by the Secretary under section 505 or section 512, or

["(ii) requires licensing by the Secretary under section 351 of the Public Health Service Act or by the Secretary of Agriculture under the Act of March 4, 1913 (known as the Virus Serum Toxin Act),

before it may be shipped in interstate commerce to a country and which does not have such approval or license shall be deemed misbranded, adulterated, and in violation of such sections or Acts unless the drug is shipped by a person only to a country described in paragraph (2) and if the drug meets the requirements of paragraphs (1)(B) and (3).

["(B) If a drug (including a biological product) described in subparagraph (A) that is manufactured, processed, packaged, or held in conformity with current good manufacturing practice and not adulterated under section 501 (a)(1), (a)(2)(A), (a)(3), (c) or (d) is shipped by a person to a country in accordance with this subsection, such drug shall not be considered to be in violation of section 505 or 512, section 351 of the Public Health Service Act, or the Act of March 4, 1913 (known as the Virus Serum Toxin Act), and shall not be deemed to be adulterated or misbranded for purposes of this Act.

["(2)(A) A drug described in paragraph (1) may be shipped to—

["(i) a developed country which is on the list established by the Secretary and which has an adequate governmental health authority to approve drugs including—

["(I) regulatory procedures to assure adequate scientific review of the animal and clinical studies relating to the safety and effectiveness of drugs before drugs are approved for marketing;

["(II) regulatory procedures to assure that labeling information provided in such country to physicians, pharmacists and patients is accurate and conforms with the laws of such country;

["(III) regulatory procedures to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

["(IV) procedures and trained personnel to administer and to enforce the policies of that authority including the capability to remove or cause to be removed from the

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market drugs which present a serious safety problem in such country; or

"(ii) a developed country which is on the list established by the Secretary and which has an adequate governmental health authority—

"(I) to assure that labeling information provided in such country to physicians, pharmacists and patients accurately reflects and is consistent with the labeling for the drug approved or licensed by a country on the list established by the Secretary under clause (i);

"(II) to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

"(III) which has procedures and personnel sufficient to administer and to enforce the policies of that authority including the capability to remove or cause to be removed from the market drugs which present a serious safety problem in such country; or

"(iii) a country which is not included on the list established by the Secretary in clause (i) or (ii) if the Secretary determines that, on the basis of scientific evidence including clinical investigations, the shipment of such drug to such country is justified to promote the public health in such country because of diseases (such as tropical diseases) or particular health conditions in such country which do not exist to a significant extent in the United States.

"(B) Within ninety days after the date of enactment of this subsection, the Secretary shall establish the lists of countries required by clauses (i) and (ii) of subparagraph (A).

"(C) The Secretary shall periodically revise the lists of countries established under clauses (i) and (ii) of subparagraph (A).

"(D) In establishing and revising the lists of countries under clauses (i) and (ii) of subparagraph (A), the Secretary—

"(i) shall consult with independent experts in the field of drug regulation; and

"(ii) shall provide reasonable opportunity for public comment before such lists are established or revised.

"(3) A drug described in paragraph (1) may be shipped by a person to a country on a list established under clause (i) or (ii) of paragraph (2)(A) or a country described in clause (iii) of such paragraph only if—

"(A) the drug meets the requirements of subparagraphs (A) through (D) of subsection (d)(1);

"(B) the drug is not the subject of final action by the Secretary or the Secretary of Agriculture denying, withdrawing, or suspending approval or licensing or otherwise banning the drug on the basis of safety and effectiveness;

"(C) the drug is not the subject of a notice by the Secretary or Secretary of Agriculture of a determination that the manufacture of the drug in the United States for shipment to a country is contrary to the public health and safety in the United States;

"(D) in the case of a drug to be shipped to a country on the list established under clause (ii) of paragraph (2)(A) or a coun-

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try described in clause (iii) of such paragraph, the drug (or drug containing the same active ingredient or ingredients) is the subject of—

[“(i) a current application for exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

[“(ii) an application for approval or licensing as described in paragraph (1)(A); or

[“(iii) a current drug master file containing all safety information required to be included in an application for an exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

[“(E) in the case of a drug to be shipped to a developed country on the list established under clause (ii) of paragraph (2)(A)—

[“(i) the drug has been approved or licensed by a country included on the list established under paragraph (2)(A)(i);

[“(ii) the labeling of the drug accurately reflects and is consistent with the labeling for such drug approved or licensed by a country on the list established under paragraph (2)(A)(i);

[“(iii) the labeling is in an appropriate language for the importing country; and

[“(iv) the drug is not the subject of an action by a governmental health authority in a country on a list established under clause (i) of paragraph (2)(A) denying or withdrawing approval or licensing or otherwise banning the drug on the basis of safety;

[“(F) the person seeking to ship the drug has complied with paragraph (4) with respect to such drug; and

[“(G) the outside of the shipping package is labeled to state ‘This drug may be sold or offered for sale only in the following countries:’ and is followed by a list of the countries to which shipment is authorized under this subsection.

[“(4)(A) A person seeking to ship a drug pursuant to this subsection shall submit to the Secretary or the Secretary of Agriculture, at least ninety days prior to the date of the first shipment of the drug, a notice of intent to ship such drug. Within fifteen days of receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which shall identify the drug to be shipped and state the country or countries to which the drug will be shipped.

[“(B) A person who has met the requirements of this subsection with respect to a drug including submitted a notice under subparagraph (A) and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(i), which country was not included in the notice submitted under subparagraph (A), shall submit to the Secretary or Secretary of Agriculture, at least fourteen days prior to the date of the first shipment of the drug to that country, a notice of intent to ship.

[“(C) A person who has met the requirements of this subsection with respect to a drug and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(ii) for which he

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has not submitted a notice shall submit to the Secretary or Secretary of Agriculture, at least thirty days prior to the date of the first shipment of the drug to that country, a notice of intent to ship. Within fifteen days of receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which shall identify the drug to be shipped and state the country to which the drug will be shipped.

"(D) The notice of intent to ship submitted to the Secretary or Secretary of Agriculture shall—

"(i) identify the drug to be shipped;

"(ii) identify the establishment where the drug has been or will be manufactured;

"(iii) identify the country or countries to which such person will ship the drug;

"(iv) in the case of a drug to be shipped to a country on the list established under paragraph (2)(A)(ii), include a copy of the labeling described in paragraph (3)(E)(ii);

"(v) include, to the extent not in conflict with the was of the foreign country, to which the drug is intended for export, a written agreement from each importer to whom the drug is to be shipped from the United States that such importer will not ship the drug to a country to which the drug may not be shipped under the requirements of paragraph (2)(A) unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture; and

"(vi) include assurances that, to the extent not otherwise required under this Act, reports of serious adverse drug reactions known to the person shipping the drug from the United States shall be transmitted promptly to the Secretary for inclusion in a drug master file.

The written agreement required under clause (v) shall be renewed annually or upon the next shipment if such shipment occurs later than one year from the date of the first agreement submitted under this paragraph.

"(5)(A) Within sixty days after a person submits a notice with respect to a drug under paragraph (4)(A), the Secretary or the Secretary of Agriculture may determine that a proposed shipment of a drug does not comply with all the requirements of paragraphs (1) to (4) of this subsection. If the Secretary or the Secretary of Agriculture makes such a determination, the Secretary or the Secretary of Agriculture shall, at the time of such determination, provide such person with a written statement specifying—

"(i) the deficiencies which such person must correct in order to enable such shipment to comply with such requirements; and

"(ii) that such person has a reasonable opportunity to correct such deficiencies within sixty days after receiving such statement.

"(B) If a person who has received a statement under subparagraph (A) does not correct the deficiencies specified in such statement within sixty days after receiving such statement, the Secretary or the Secretary of Agriculture may issue an order stating that the shipment of a drug with respect to which such statement

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was made does not comply with all the requirements of this subsection and prohibiting such shipment.

["(6)(A) Except as provided in subparagraphs (B) and (C), at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of Agriculture may determine that such shipment is unlawful because such shipment does not comply with any requirement of paragraph (3), and may issue an order to prohibit such shipment.

["(B) If, at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of Agriculture determines that such shipment does not comply with subparagraph (A) of paragraph (3) or subparagraphs (C) through (F) of such paragraph, the Secretary or the Secretary of Agriculture shall, prior to issuing an order with respect to such shipment under subparagraph (A) of this paragraph, provide the person who submitted the notice under paragraph (4) with respect to such shipment with a written statement which—

["(i) specifies such determination; and

["(ii) states that such person may, within thirty days after receiving such statement, take such action as the Secretary or the Secretary of Agriculture determines necessary to comply with the requirements of subparagraph (A), (C), (D), (E), or (F) of paragraph (3), as the case may be, in order to permit the shipment of such drug.

["(C) If the Secretary or the Secretary of Agriculture determines that the person who receives a statement under subparagraph (B) does not take the action required by the Secretary or the Secretary of Agriculture under clause (ii) of such subparagraph, or that such person takes an action which is inadequate to comply with the requirement of subparagraph (A), (C), (D), (E) or (F) of paragraph (3), as the case may be, the Secretary or the Secretary of Agriculture shall issue an order under subparagraph (A) with respect to such drug. Any such order shall be accompanied by a written statement—

["(i) specifying each requirement of paragraph (3) which has not been complied with relating to such shipment; and

["(ii) stating that the person who is the subject of such order will be provided, on request, with an opportunity for an informal hearing with respect to such order.

["(7) The Secretary, or in his absence the officer acting as Secretary, may prohibit the shipping of a drug to a country or countries authorized under this subsection if the drug has been determined by the Secretary of Agriculture to present an imminent hazard to the public health in such country or countries. The authority conferred by this paragraph shall not be delegated by the Secretary. A determination by the Secretary or the Secretary of Agriculture under this paragraph shall not be stayed pending final action by a reviewing court.

["(8)(A) If at any time the Secretary, or in his absence the officer acting as Secretary, determines that a person is shipping a drug from the United States to an importer which importer is shipping the drug to a country to which shipment is not authorized and that such shipment presents an imminent hazard to public health in the unauthorized country, then the Secretary shall immediately

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prohibit the shipping of the drug to such importer, give the person shipping the drug from the United States prompt notice of the determination, and afford such person an opportunity for an expedited hearing.

"(B) If the Secretary, or in his absence the officer acting as Secretary, receives credible evidence that a drug shipped to a country authorized under paragraph (2)(A) has been or is being shipped to a country not authorized under paragraph (2)(A) and if, upon investigation, the Secretary determines that there is a reasonable basis to believe that such drug has been so shipped, then the Secretary shall immediately—

"(1) notify the governments of the countries involved; and

"(2) notify any person shipping the drug from the United States of the shipment of the drug to a country to which shipment is not authorized.

"(C) Any person receiving the notification under subparagraph (B) shall investigate the matter and report to the Secretary within fourteen days his findings, if any, regarding the source and cause of the shipment of the drug to a country to which shipment is not authorized and the steps the person is taking to remedy any noncompliance with the terms of the importer agreement required under paragraph (4)(E)(v).

"(D) If, sixty days after receiving the findings under subparagraph (C), the Secretary, or in his absence the officer acting as Secretary, determines that despite the efforts taken under subparagraph (C), the person who imported the drug from the United States is continuing to ship the drug to a country to which shipment is not authorized, then the Secretary shall prohibit the shipping of the drug to such importer.

"(E) If—

"(1) the person shipping the drug from the United States has been notified under subparagraph (A) that it presents an imminent hazard, such person continues to ship such drug from the United States to a prohibited importer, or

"(2) sixty days after the Secretary receives the findings under subparagraph (C), a person continues to ship a drug from the United States to an importer knowing that the importer is continuing to ship the drug to a country to which shipment is not authorized,

then the drug shall be deemed to be misbranded and shall not be shipped unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture.

"(F) The authority conferred by this paragraph shall not be delegated by the Secretary.".

SEC. 4. The list of countries initially established by the Secretary of Health and Human Services under section 801(e)(2)(A)(i) of the Federal Food, Drug, and Cosmetic Act (as added by section 2 of this Act) shall include the following countries unless the Secretary determines that a country should not be included on such list because the country does not have an adequate health authority to approve drugs:

(a) Australia,

(b) Austria,

(c) Belgium,

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[(d) Canada,
[(e) Denmark,
[(f) Federal Republic of Germany,
[(g) Finland,
[(h) France,
[(i) Japan,
[(j) The Netherlands,
[(k) New Zealand,
[(l) Norway,
[(m) Sweden,
[(n) Switzerland, and
[(o) The United Kingdom.

[SEC. 5. (a) Within three years of the date of enactment of the Pharmaceutical Export Amendments of 1985 and every two years thereafter, the Comptroller General shall complete a study of and transmit to the Congress and to the Secretary of Health and Human Services his findings and recommendations on—

[(1) the extent to which drugs shipped under the Pharmaceutical Export Amendments of 1985 are introduced into countries not authorized to receive such drugs by such law, and the effect of such shipment, if any, on the health of the population of such country; and

[(2) the extent to which labeling of drugs shipped under such law to countries included on the list established under section 801(e)(2)(A)(ii) of the Federal Food, Drug, and Cosmetic Act is consistent with the labeling for such drugs approved or licensed by countries on the list established under section 801(e)(2)(A)(i) of such Act.

[(b) The Secretary of Health and Human Services shall enter into a contract with the National Academy of Sciences whereby the latter will undertake a study of—

[(1) the economic impact of the Pharmaceutical Export Amendments of 1985 on employment, capital investment, and trade; and

[(2) the effect upon international health of the Pharmaceutical Export Amendments of 1985.

The Academy shall transmit its findings to the Congress within five years of the date of enactment.

[SEC. 6. (a) Section 526(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb(a)(2) is amended by inserting "(including a disease or condition prevalent in a developing country)" after "any disease or condition".

[(b) Section 5(b)(2) of the Orphan Drug Act (21 U.S.C. 360ee(b)(2) is amended by inserting "(including a disease or condition prevalent in a developing country)" after "any disease or condition".

That this Act may be cited as the "Pharmaceutical Export Amendments of 1986".

SEC. 2. (a) The Congress finds that—

(1) the development and international distribution of safe and effective pharmaceutical products by United States-based firms promotes world health and is important to the national economy;

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(2) the policy governing worldwide distribution of pharmaceutical products manufactured in the United States should promote the public health;

(3) the full public health benefits that could be afforded by new drugs manufactured in the United States are at times unnecessarily limited by the export restrictions which exist under United States law;

(4) the current law of the United States does not permit the export of such drugs prior to approval in the United States;

(5) there are other developed countries which have sophisticated health regulatory authorities which protect the health and safety of their citizens;

(6) many new drugs developed by United States pharmaceutical companies are approved for marketing in such foreign countries prior to approval in the United States;

(7) the inability to export such drugs to countries which have adequate regulatory authorities especially hinders the international competitiveness of smaller United States firms and firms in the biotechnology field from entering foreign markets directly, and often such entrance is only possible through technology licensing agreements with foreign competitor manufacturers;

(8) it is appropriate to permit the export of new drugs to countries in which they are approved under circumstances that protect against harm to the health or safety of citizens in the importing country;

(9) the inability to export drugs approved abroad discourages investment in the United States, results in the loss of employment opportunities in this country, and erodes the favorable balance of trade in pharmaceuticals; and

(10) it is appropriate to provide sufficient safeguards to ensure that drugs so exported are not diverted to countries that may not have adequate drug regulatory authorities.

(b) The purposes of this Act are—

(1) to permit the shipment of new drugs prior to approval in the United States to certain developed countries that meet certain specified regulatory standards;

(2) to protect against the diversion of such drugs to countries that do not have highly sophisticated health regulatory authorities;

(3) to encourage the development and availability of drugs to treat diseases or health conditions which are rare in the United States;

(4) to encourage new capital investment, the creation of new job opportunities in the United States, and maintain the favorable trade balance in pharmaceuticals; and

(5) to enable the United States biotechnology industry to enter foreign markets to the extent permitted by foreign law without licensing their technology to foreign firms.

SEC. 3. Section 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381) is amended by adding at the end thereof the following new subsection:

"(e)(1)(A) A drug (including a biological product) intended for human or animal use which—

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"(i) requires approval by the Secretary under section 505 or section 512, or

"(ii) requires licensing by the Secretary under section 351 of the Public Health Service Act or by the Secretary of Agriculture under the Act of March 4, 1913 (known as the Virus Serum Toxin Act),

before it may be shipped in interstate commerce to a country and which does not have such approval or license shall be deemed misbranded, adulterated, and in violation of such sections or Acts unless the drug is shipped by a person only to a country described in paragraph (2) and if the drug meets the requirements of subparagraph (B) and paragraph (3).

"(B) If a drug (including a biological product) described in subparagraph (A) that is manufactured, processed, packaged, or held in conformity with current good manufacturing practice and that is not adulterated under subsection (a)(1), (a)(2)(A), (a)(3), (c), or (d) of section 501 is shipped by a person to a country in accordance with this subsection, such drug shall not be considered to be in violation of section 505 or 512, section 351 of the Public Health Service Act, or the Act of March 4, 1913 (known as the Virus Serum Toxin Act), and shall not be deemed to be adulterated or misbranded for purposes of this Act.

"(2)(A) A drug described in paragraph (1) may be shipped to—

"(i) a developed country which is on the list established by the Secretary of countries which have an adequate governmental health authority to approve drugs including—

"(I) regulatory procedures to assure adequate scientific review of the animal and clinical studies relating to the safety and effectiveness of drugs before drugs are approved for marketing;

"(II) regulatory procedures to assure that labeling information provided in such country to physicians, pharmacists, and patients is accurate and conforms with the laws of such country;

"(III) regulatory procedures to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

"(IV) procedures and trained personnel to administer and to enforce the policies of that authority, including the capability to remove or cause to be removed from the market drugs which present a serious safety problem in such country; or

"(ii) a developed country which is on the list established by the Secretary of countries which have an adequate governmental health authority—

"(I) to assure that labeling information provided in such country to physicians, pharmacists, and patients accurately reflects, and is consistent with, the labeling for the drug approved or licensed by a country on the list established by the Secretary under clause (i);

"(II) to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

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"(III) which has procedures and personnel sufficient to administer and to enforce the policies of that authority, including the capability to remove or cause to be removed from the market drugs which present a serious safety problem in such country; or

"(iii) a country which is not included on the list established by the Secretary under clause (i) or (ii) if the Secretary determines that, on the basis of scientific evidence including clinical investigations, the shipment of such drug to such country is justified to promote the public health in such country because of diseases (such as tropical diseases) or particular health conditions in such country which do not exist to a significant extent in the United States.

"(B) Within ninety days after the date of enactment of this subsection, the Secretary shall establish the lists of countries required by clauses (i) and (ii) of subparagraph (A).

"(C) The Secretary shall periodically revise the lists of countries established under clauses (i) and (ii) of subparagraph (A).

"(D) In establishing and revising the lists of countries under clauses (i) and (ii) of subparagraph (A), the Secretary—

"(i) shall consult with independent experts in the field of drug regulation; and

"(ii) shall provide reasonable opportunity for public comment before such lists are established or revised.

"(3) A drug described in paragraph (1) may be shipped by a person to a country on a list established under clause (i) or (ii) of paragraph (2)(A) or a country described in clause (iii) of such paragraph only if—

"(A) the drug meets the requirements of subparagraphs (A) through (D) of subsection (d)(1);

"(B) the drug is not the subject of final action by the Secretary or the Secretary of Agriculture denying, withdrawing, or suspending approval or licensing or otherwise banning the drug on the basis of safety and effectiveness;

"(C) the drug is not the subject of a notice by the Secretary or Secretary of Agriculture of a determination that the manufacture of the drug in the United States for shipment to a country is contrary to the public health and safety in the United States;

"(D) in the case of a drug to be shipped to a country on the list established under clause (ii) of paragraph (2)(A) or a country described in clause (iii) of such paragraph, the drug (or a drug containing the same active ingredient or ingredients) is the subject of—

"(i) a current application for exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

"(ii) an application for approval or licensing as described in paragraph (1)(A); or

"(iii) a current drug master file containing all safety information required to be included in an application for an exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

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"(E) in the case of a drug to be shipped to a developed country on the list established under clause (ii) of paragraph (2)(A)—

"(i) the drug has been approved or licensed by a country included on the list established under clause (i) of paragraph (2)(A);

"(ii) the labeling of the drug accurately reflects and is consistent with the labeling for such drug approved or licensed by a country on the list established under clause (i) of paragraph (2)(A);

"(iii) the labeling is in an appropriate language for the importing country; and

"(iv) the drug is not the subject of an action by a governmental health authority in a country on the list established under clause (i) of paragraph (2)(A) denying or withdrawing approval or licensing or otherwise banning the drug on the basis of safety;

"(F) the person seeking to ship the drug has complied with paragraph (4) with respect to such drug; and

"(G) the outside of the shipping package of such drug is labeled with the following statement: 'This drug may be sold or offered for sale only in the following countries:

.', the blank space therein being filled with a list of the countries to which shipment of the drug is authorized under this subsection.

"(4)(A) A person seeking to ship a drug pursuant to this subsection shall submit to the Secretary or the Secretary of Agriculture, at least ninety days prior to the date of the first shipment of the drug, a notice of intent to ship such drug. Within fifteen days after receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which identifies the drug to be shipped and states each country to which the drug will be shipped.

"(B) A person who has met the requirements of this subsection with respect to a drug including the submission of a notice under subparagraph (A) and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(i), which country was not included in the notice submitted under subparagraph (A), shall submit to the Secretary or Secretary of Agriculture, at least fourteen days prior to the date of the first shipment of the drug to that country, a notice of intent to ship.

"(C) A person who has met the requirements of this subsection with respect to a drug and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(ii) for which such person has not submitted a notice under subparagraph (A) with respect to such drug shall submit to the Secretary or Secretary of Agriculture, at least thirty days prior to the date of the first shipment of the drug to that country, a notice of intent to ship. Within fifteen days of receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which identifies the drug to be shipped and states the country to which the drug will be shipped.

"(D) Any notice of intent to ship submitted to the Secretary or Secretary of Agriculture under this paragraph shall—

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"(i) identify the drug to be shipped;

"(ii) identify the establishment where the drug has been or will be manufactured;

"(iii) identify each country to which such person will ship the drug;

"(iv) in the case of a drug to be shipped to a country on the list established under paragraph (2)(A)(ii), include a copy of the labeling described in paragraph (3)(E)(ii);

"(v) include, to the extent not in conflict with the laws of the country to which the drug is intended for export, a written agreement from each importer to whom the drug is to be shipped from the United States that such importer will not ship the drug to a country to which the drug may not be shipped under the requirements of paragraph (2)(A) unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture; and

"(vi) include assurances that, to the extent not otherwise required under this Act, reports of serious adverse drug reactions known to the person shipping the drug from the United States shall be transmitted promptly to the Secretary for inclusion in a drug master file.

The written agreement required under clause (v) shall be renewed annually or upon the next shipment if such shipment occurs later than one year from the date of the first agreement submitted under this paragraph.

"(5)(A) Within sixty days after a person submits a notice of intent to ship with respect to a drug under paragraph (4)(A), the Secretary or the Secretary of Agriculture may determine that a proposed shipment of a drug does not comply with all the requirements of paragraphs (1) through (4). If the Secretary or the Secretary of Agriculture makes such a determination, the Secretary or the Secretary of Agriculture shall, at the time of such determination, provide such person with a written statement specifying—

"(i) the deficiencies which such person must correct in order to enable such shipment to comply with such requirements; and

"(ii) that such person has a reasonable opportunity to correct such deficiencies within sixty days after receiving such statement.

"(B) If a person who has received a statement under subparagraph (A) does not correct the deficiencies specified in such statement within sixty days after receiving such statement, the Secretary or the Secretary of Agriculture may issue an order stating that the shipment of a drug with respect to which such statement was made does not comply with all the requirements of this subsection and prohibiting such shipment.

"(6)(A) Except as provided in subparagraphs (B) and (C), at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of Agriculture may determine that such shipment is unlawful because such shipment does not comply with any requirement of paragraph (3), and may issue an order to prohibit such shipment.

"(B) If, at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of

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Agriculture determines that such shipment does not comply with subparagraph (A) of paragraph (3) or subparagraphs (C) through (F) of such paragraph, the Secretary or the Secretary of Agriculture shall, prior to issuing an order with respect to such shipment under subparagraph (A) of this paragraph, provide the person who submitted the notice under paragraph (4) with respect to such shipment with a written statement which—

"(i) specifies such determination; and

"(ii) states that such person may, within thirty days after receiving such statement, take such action as the Secretary or the Secretary of Agriculture determines necessary to comply with the requirements of subparagraph (A), (C), (D), (E), or (F) of paragraph (3), as the case may be, in order to permit the shipment of such drug.

"(C) If the Secretary or the Secretary of Agriculture determines that the person who receives a statement under subparagraph (B) does not take the action required by the Secretary or the Secretary of Agriculture under clause (ii) of such subparagraph, or that such person took an action which is inadequate to comply with the requirement of subparagraph (A), (C), (D), (E) or (F) of paragraph (3), as the case may be, the Secretary or the Secretary of Agriculture shall issue an order under subparagraph (A) with respect to such drug. Any such order shall be accompanied by a written statement—

"(i) specifying each requirement of paragraph (3) which has not been complied with relating to such shipment; and

"(ii) stating that the person who is the subject of such order will be provided, on request, with an opportunity for an informal hearing with respect to such order.

"(7) The Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, may prohibit the shipping of a drug to a country or countries authorized under this subsection if the drug has been determined by such Secretary or officer to present an imminent hazard to the public health in such country or countries. A determination by such Secretary or officer under this paragraph shall not be stayed pending final action by a reviewing court. The authority conferred by this paragraph to prohibit the shipment of a drug shall not be delegated by the Secretary or the Secretary of Agriculture, except that in the case of the absence of either such Secretary, such authority may be delegated to the officer acting as such Secretary.

"(8)(A) If at any time the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, determines that—

"(i) a person is shipping a drug from the United States to an importer;

"(ii) such importer is shipping the drug to a country to which shipment is not authorized under this subsection; and

"(iii) such shipment presents an imminent hazard to public health in the country to which shipment is not authorized under this subsection,

such Secretary or officer shall immediately prohibit the shipment of the drug to such importer, give the person shipping the drug

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from the United States prompt notice of the determination, and afford such person an opportunity for an expedited hearing.

"(B) If the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, receives credible evidence that a drug shipped to a country to which shipment is authorized under paragraph (2)(A) has been or is being shipped to a country to which shipment is not authorized under paragraph (2)(A) and if, upon investigation, such Secretary or officer determines that there is a reasonable basis to believe that such drug has been so shipped, such Secretary or officer shall immediately—

"(i) notify the governments of the countries involved; and

"(ii) notify any person shipping the drug from the United States of the shipment of the drug to a country to which shipment is not authorized.

"(C) Any person receiving notification under subparagraph (B) shall investigate the matter and report to the Secretary or the Secretary of Agriculture within fourteen days the findings of such person, if any, regarding the source and cause of the shipment of the drug to a country to which shipment is not authorized under this subsection and the steps the person is taking to remedy any noncompliance with the terms of the importer agreement required under paragraph (4)(D)(v).

"(D) If, sixty days after receiving the findings under subparagraph (C), the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, determines that despite the efforts taken under subparagraph (C), the person who imported the drug from the United States is continuing to ship the drug to a country to which shipment is not authorized under this subsection, then such Secretary or officer shall prohibit the shipping of the drug to such importer.

"(E) If—

"(i) a person shipping a drug from the United States has been notified under subparagraph (A) that the shipment of the drug presents an imminent hazard, and such person continues to ship such drug from the United States to a prohibited importer, or

"(ii) sixty days after the Secretary receives the findings under subparagraph (C), a person continues to ship a drug from the United States to an importer knowing that the importer is continuing to ship the drug to a country to which shipment is not authorized,

then the drug shall be deemed to be misbranded and shall not be shipped unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture.

"(F) The authority conferred by this paragraph shall not be delegated by the Secretary or the Secretary of Agriculture.".

SEC. 4. The list of countries initially established by the Secretary of Health and Human Services under section 801(e)(2)(A)(i) of the Federal Food, Drug, and Cosmetic Act (as added by section 3 of this Act) shall include the following countries unless the Secretary determines that a country should not be included on such list because the country does not have an adequate health authority to approve drugs:

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Australia.
Austria.
Belgium.
Canada.
Denmark.
Federal Republic of Germany.
Finland.
France.
Japan.
The Netherlands.
New Zealand.
Norway.
Sweden.
Switzerland.
The United Kingdom.

SEC. 5. (a) Within two years after the date of enactment of this Act and every two years thereafter, the Comptroller General of the United States shall complete a study of, and transmit to the Congress and to the Secretary of Health and Human Services the findings and recommendations of the Comptroller General on—

(1) the extent to which drugs shipped under section 801(e) of the Federal Food, Drug, and Cosmetic Act (as added by section 3 of this Act) are introduced into countries not authorized to receive such drugs by such section, and the effect of such shipment, if any, on the health of the population of such country; and

(2) the extent to which labeling of drugs shipped under such law to countries included on the list established under section 801(e)(2)(A)(ii) of the Federal Food, Drug, and Cosmetic Act (as added by section 3 of this Act) is consistent with the labeling for such drugs approved or licensed by countries on the list established under section 801(e)(2)(A)(i) of such Act (as added by section 3 of this Act).

(b)(1) The Secretary of Health and Human Services shall enter into a contract with the National Academy of Sciences whereby the National Academy of Sciences will undertake a study of—

(A) the economic impact of the provisions of section 801(e) of the Federal Food, Drug, and Cosmetic Act (as added by section 3 of this Act) on employment, capital investment, and trade; and

(B) the effect upon international health of the provisions of such section 801(e).

(2) The contract entered into under paragraph (1) shall contain provisions requiring the National Academy of Sciences to transmit its findings under this subsection to the Congress within five years after the date of enactment of this Act.

(3) The contract entered into under paragraph (1) shall be to such extent or in such amounts as are provided in appropriation Acts.

SEC. 6. (a) Section 526(a)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb(a)(2) is amended by inserting "(including a disease or condition prevalent in a developing country)" after "any disease or condition".

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(b) Section 5(b)(2) of the Orphan Drug Act (21 U.S.C. 360ee(b)(2) is amended by inserting "(including a disease or condition prevalent in a developing country)" after "any disease or condition".

SEC. 7. Section 402(d)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(d)(2)) is amended by inserting before the semicolon "except that this clause shall not apply to confectionery which is introduced or delivered for introduction into, or received or held for sale in, interstate commerce if the sale of such confectionery is permitted under the laws of the State in which such confectionery is intended to be offered for sale".

SEC. 8. The provisions of this Act and of the amendments made by this Act do not authorize the appropriation of any funds for fiscal year 1986.

IV. COMMITTEE HEARINGS

A hearing was held before the full Committee on Labor and Human Resources on June 28, 1984. Oral testimony was received from:

Dr. Mark Novitch, Acting Commissioner of Food and Drugs.

Lewis Engman, President, Pharmaceutical Manufacturers Association.

John E. Robson, Executive Vice-President, G.D. Searle.

Robert A Ingram, Vice-President for Public Affairs, Merrell Dow Pharmaceuticals.

Robert A. Swanson, President, Genentec Inc.

Verne William, Member, Executive Committee, Johnson and Johnson.

John R. Stafford, President, American Home Products.

Irwin Lerner, President/Chief Executive Officer, Hoffmann-LaRoche, Inc.

William F. Haddad, President and Chief Executive Officer, Generic Pharmaceutical Industry Association.

Louise Greenfield, Staff Attorney, Public Citizens' Congress Watch.

Dr. Sidney Wolfe, Public Citizen Health Research Group.

Written testimony by the following was also received:

American Cyanamid Company.

Consumers Union.

Miles Laboratories, Inc.

Richard Miller, Research Associate, the Labor Institute.

National Resources Defense Council, Inc.

Sybil Shainwald.

Dr. Philip R. Lee, Institute for Health Policy Studies, University of California at San Francisco.

A further hearing was held before the full Committee on June 5, 1985. Oral testimony was received from:

Dr. Frank E. Young, Commissioner, Food and Drug Administration; Dr. Stewart Nightingale, Associate Commissioner for Medical Affairs; and Thomas Scarlett, General Counsel of the Food and Drug Administration.

Gerald J. Mossinghoff, President, Pharmaceutical Manufacturers Association.

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David B. Sharrock, President, Merrell-Dow Pharmaceuticals, U.S.A.

Robert A. Swanson, President, Genentech, Inc.

Tim Hart, Executive Director, Association of Biotechnology Companies.

Dr. Paulo de Almeida Machado, Former Minister of Health of Brazil.

C. Payne Lucas, Executive Director, Africare.

Alan Alemian, Regional Development Officer, Eastern and Southern Regions of Africa, Africare.

Humphrey Taylor, President, Louis Harris and Associates, Inc.

Dr. Sidney M. Wolfe, Director, Public Citizens' Health Research Group.

Nancy Drabble, Director, Public Citizens' Congress Watch.

Written statements were also received from:

Dr. Ronald E. Cape, Chairman and Chief Executive Officer, Cetas Corporation, and President, Industrial Biotechnology Association.

Merc and Company, Inc.

Richard D. Miller, Research Associate, the Labor Institute.

Ambassador Michael B. Smith, acting United States Trade Representative.

American Cyanamid Company.

Dr. Philip Lee, Institute for Health Policy Studies, University of California at San Francisco.

V. Committee Views

As pointed out in Section II, S. 1848, the Pharmaceutical Export Amendments of 1985, addresses an issue of longstanding interest and concern to the members of this Committee. This particular vehicle has seen numerous stages of refinement, and now enjoys the support of an overwhelming bipartisan majority of Committee members.

Section 3 of the legislation is the heart of the proposal. It adds a new subsection (e) to Section 801 of the Federal Food, Drug, and Cosmetic Act (FFDCA) to permit the export of certain unapproved products under limited conditions.

Paragraph (1) of subsection 801(e) applies to any drug, including a biological product, which is not approved or licensed and which, prior to distribution in interstate commerce, must be approved or licensed under Sections 505 or 512 of FFDCA, Section 351 of the Public Health Service Act (PHSA), or the Virus Serum Toxin Act (VS&T). Such a drug is deemed misbranded, adulterated or in violation of the foregoing provisions unless: 1) the drug is manufactured, processed, packaged and/or held in conformity with current good manufacturing practice; (2) the drug is not adulterated under subsections (a)(1), (a)(2)(A), (a)(3), (c), or (d) of Section 501 of the FFDCA; (3) the drug is shipped only to a country described in paragraph (2); and (4) the shipment of the drug meets the conditions specified in paragraph (3). The Committee notes that although the adulteration provision of Section 501(a)(4) is not mentioned in the amendments, it does not intend this new authority to permit ship-

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ment abroad of color additives which may not be legally used in the importing country.

The Committee assumes that foreign nations on the first tier list impose their own review and requirements on color additives. It acknowledges that different countries' regulations may very, and imposition of a single approach may not be appropriate. The Committee does not suggest that dangerous color additives should be exported under these amendments.

If a person ships an unapproved drug for sale which does not meet all four of the above conditions, then the drug is deemed to be misbranded, adulterated, or in violation of the applicable section or Act.

The Committee intends for current law to apply in the enforcement of these amendments. Generally, under existing law, FDA has inspection authority to investigate compliance with the FFDCA and enforcement authority to bring seizure or injunction actions, or to institute criminal prosecution, for any violation of the FFDCA. USDA has comparable criminal authority.

These amendments permit the export of drugs as an exception to the respective acts. If all of the conditions established by these amendments for export of particular drugs are not met, the exemption for export would be inapplicable and any export would automatically represent a violation of the existing drug provisions of the law and thus would be subject to the existing civil and criminal penalties under the respective Acts. For example, in the case of products subject to FFDCA, the shipment of a drug which was not made in conformity with current good manufacturing practices would be a prohibited act under Section 301. As such, the FDA could take the appropriate remedial measures under Sections 302, 303, and 304 of the FFDCA. Other enforcement authorities are provided in paragraphs (7) and (8) of subsection (e) and are explained elsewhere.

Paragraph (2)(A) of Section 801(e) describes the three categories of countries to which drugs referred to in paragraph (1) may be shipped. The Secretary of Health and Human Services is required to establish lists of those countries which meet the criteria of the first two categories.

The first list includes those developed countries ("first tier countries") which have premarketing drug approval requirements comparable to those of the FDA. There are four criteria for the first group of countries. The four criteria are intended to outline some of the characteristics of a highly sophisticated and effective regulatory system comparable to the U.S. Food and Drug Administration.

The first criterion is adequate resources to do comprehensive scientific and medical review to determine the safety and efficacy of the drugs evaluated.

The second criterion involves labeling. All countries in this group must have sufficient resources and procedures to effectively regulate labeling so that information received by patients, physicians, and pharmacists accurately reflects the evaluation of the agency as to indications, contradictions, precautions, dosage and administration, adverse reactions, warnings, and whether the drug needs to be taken under the direction of a physician. The regulatory author-

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ity must be able to monitor and enforce such labeling requirements.

The third criterion involves detection and reporting of adverse drug reactions. The drug regulatory authority must have a system in place by which adverse drug reactions which come to the attention of physicians will be reported, collected, and reviewed by the appropriate authority.

The Committee recognizes that there are several systems for collecting these data. Some are similar to that used in the United States; others differ. In determining whether a country meets this requirement, the Committee expects the Secretary to focus on whether the data is gathered and not whether the system is identical to that of the United States.

The fourth criterion adds several additional general characteristics of an effective drug authority. The drug authority must be an operational and effective system to implement its regulatory mission. It must have personnel appropriately trained for their jobs who can administer and carry out these procedures. And it must have a meaningful and effective system to enforce the procedures as documented and implemented.

The second list of countries ("second tier countries") is composed of developed nations (other than those in the first list) which have an adequate health authority to administer several requirements. The authority must be able to assure that information provided to physicians, pharmacists, and patients accurately reflects, and is consistent with, the labeling approved for the drug by a country on the first list.

The intent of this provision is to ensure that claims of safety and efficacy are supported by scientifically reviewed clinical data so that unsupported indications will not be added, and contradictions and warnings will not be deleted from the information provided.

For example, if a drug has been approved in the United Kingdom for two indications, A and B, then it could be sold for either or both of those indications in a country on the second list. If a particular country on the second list refused to approve the B indication, then the drug could only be sold for the A indication. Even though a country on the second list is willing to approve the drug for indications A, B, and C, the drug could not be sold for all three indications unless one of the countries on the first list had approved all three.

Clearly, labeling must conform to the regulations of the importing country. Because indications and regulations may differ among countries, labels used in second tier countries may not be identical to those used in first tier countries. But, different regulations must not be an excuse for deleting information as to contraindications or warnings provided in a first tier country. Whether the drug is supposed to be taken under the direction of a physician should be included.

Like countries on the first list, those on the second list must also have an adequate health authority to detect, record and act upon serious safety problems with respect to a drug. Countries on the second list must have procedures and trained personnel to implement their regulatory authorities. The health authority must represent an operational and effective system and must be able to ad-

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minister and enforce its regulatory mission. It must have the capability to remove or cause to be removed from the market drugs which present a serious safety problem. The requirements described in this paragraph are intended to be identical to the last three characteristics of the first tier countries. It is anticipated that this second group of countries will initially be relatively small until there are advances in regulatory capabilities in other countries.

It is not the Committee's intent to define with these second tier criteria countries exhibiting impressive economic development coupled with a properly named but ineffectively run health regulatory authority. It is for this reason that the criteria speak not only to whether a country is developed but move beyond that factor to focus on the competence of its actual regulatory system.

Under the limitations of the new law, the Secretary is proscribed from including on either of these lists developing or so-called Third World nations. Under limited circumstances, however, unapproved drugs may be shipped to nations which do not meet the criteria of either the first or second list. Among these nations are developing countries with extensive health needs and insufficient resources to develop or test pharmaceutical remedies that might provide relief for their particular health needs. Unapproved drugs may be shipped to these countries ("third tier countries") if the Secretary determines that, on the basis of scientific evidence including clinical studies, the drug will promote the public health in the importing country because of particular diseases or health conditions in the importing country.

This provision is meant to cover particular situations which will be reviewed by the Secretary on a case by case basis, where particular health needs of a developing country produce a significant need for a particular drug not generally in demand in the United States. In such cases, drugs which are being researched and are in the clinical testing phase and which have been adequately evaluated so as to promise considerable benefit compared to the risk of significant adverse effects, may be exported to the countries in need.[1]

This provision is not intended to be a loophole to permit the export of drugs with little relevance to significant health needs of the countries in question. Tropical disease drugs are the principal category of pharmaceuticals this paragraph is intended to cover. In deliberating this paragraph, we took note of the fact that nine drugs included in the World Health Organization's list of essential drugs are not approved by the FDA for use in the United States. This paragraph is not intended to be a loophole for sidestepping FDA requirements to gain early access to Third World markets with drugs manufactured in the United States which will have a significant market in this country.

In implementing this provision, the Secretary is to consider only those diseases or conditions, such as tropical diseases, which do not exist to a significant extent in the United States. The Secretary is

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[1] The Committee notes that the drug designed to treat "river blindness," mentioned in the Opposing Views, has not been approved by FDA for use in humans. Because there is no market for this drug in the U.S., the manufacturer has no plans to seek FDA approval for it, and will be unable to manufacture it here for export to countries in need when the foreign clinical trials are completed and it is approved abroad, unless these amendments are enacted.

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to make such a determination based on the particular risk/benefit values appropriate to these countries.

The Committee expects that the Secretary will keep it closely advised during the development and subsequent revision of the lists of countries under the bill. It intends to monitor these lists to assure itself that the intent of the legislation is being observed.

Questions have arisen concerning the extent of the amendments' restrictions on shipment from one foreign country to another after a drug has been initially exported, the so-called "transshipment" issue.

The effect of paragraph (2)(A) is to permit a person to ship an unapproved drug from the United States to any first list country on the list established under paragraph (2)(A). In addition, the paragraph permits a person to ship such a drug from the United States to a country on the first list and then to another first tier country. Further, if a first tier country has approved a drug, a person may ship it directly from the United States to a developed country on the second list which has approved it and then onto another second tier country which has also approved it. In addition, the provision permits a person to ship such a drug from the United States to a developed country on the first list and then to a developed country on the second list if the drug otherwise qualifies for export to second tier countries. Shipment may also be made from a second tier country to a first tier country. Finally, shipment from a first or second tier country to a third tier country is permitted in those unusual circumstances where the Secretary makes the appropriate determination. These are the only permissible shipments of unapproved drugs subject to this subsection. If a person ships an unapproved drug to a country not described in paragraph (2)(A), then the drug is deemed to be misbranded, adulterated, or in violation of the applicable section or Act. For example, in the case of products subject to FFDCA, such a shipment would be a prohibited act under section 301 of the Act. Accordingly, the FDA could take the appropriate remedial measures under sections 302, 303, and 304 of the FFDCA. These penalties may include imprisonment and fines up to $100,000.

The Committee notes, however, that it is impractical to try to extend the reach of U.S. laws into the internal commerce of foreign nations, in an attempt to prevent situations which occur freely under current law. Indeed compared to current law, the provisions of these amendments give the regulatory arm of the U.S. government increased control over drugs which will otherwise be completely outside of its jurisdiction.

Additional enforcement authorities are provided in paragraphs (7) and (8) and are explained in the discussion of those provisions.

In fashioning the language governing shipments, the Committee has used the word "person" purposefully. The term is defined in Title I, Section I of the United States Code to include corporations and their subsidiaries. In implementing this provision, the Committee intends that the term include not only a corporation located in the United States but also a foreign subsidiary which is controlled by the U.S. corporation.

Further, the amendments give the Secretary the ability to monitor foreign adverse reaction reports for the drug, review ongoing

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studies, and to halt shipments in many circumstances. By way of contrast, currently the Secretary has no contact at all with a drug produced by a U.S. manufacturer overseas for foreign sale, unless the drug also happens to have been submitted in an IND or an NDA in this country. Again, the amendments increase FDA control over these products when compared to current law.

The Committee feels strongly that U.S. companies should not be engaged in unauthorized shipments of drugs under these amendments, and should be made fully responsible for exercising the contractual control available to them under the importer agreement required in Section 801(e)4. This may include insistence that the importer stop shipping the drug to an unauthorized country or termination of the import agreement if necessary. The Committee expects prompt and good faith compliance with all the duties required of exporting companies.

To further monitor actual practices under the new authority, the Committee has provided for continuing studies by the Comptroller General. These studies will reveal the extent of compliance by exporters, the extent to which drugs shipped under the new authority are introduced into countries not authorized to receive them, and any impact of the amendments on the health of foreign consumers. Further, the bill calls for the Secretary of Health and Human Services to enter into a contract with the National Academy of Sciences to assess the economic impact of the bill on employment, trade, and capital investment, and its impact on international health. It is noted that no funds are authorized for FY 1986 for either this GAO study or for the study by the National Academy of Sciences. The Committee, nevertheless, expects these studies to move forward and directs the Secretary and the Comptroller General to provide for expenses incurred during FY 1986 from existing funds.

In order to ens .re that only responsible drugs are exported under the amendments, the proposed Section 801(e)(3) sets forth a list of requirements which must be met before the drug may be shipped. Among these are a requirement that neither of the Secretaries has taken final action to deny, withdraw, or suspend approval or licensing or otherwise ban the drug on the basis of safety and effectiveness.

During the course of FDA and USDA review of new drugs, applications and petitions are frequently declared incomplete and additional testing is routinely required. At other times, agency review of applications cannot be completed within the statutory time limits and the agency will give the applicant the choice of withdrawing the application and resubmitting it, thus recommencing the statutory time period, or having the agency decide it needs more information and deny it in its current form, with leave to resubmit it, yielding the same effect on the time limits. While the Committee does not condone agency failure to meet statutory times tables, it recognizes that drug approval in this country is, in short, a continuous, evolving process. It is not intended that these intermediate steps be sufficient to stop export under the amendments. Only a final action by FDA or USDA, after all legal appeals have been exhausted, determining a drug to be unsafe or ineffective for VS&T Act, IND, INAD, NDA or NADA purposes would be sufficient to trigger the prohibition against exportation.

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Further, the drug must be labeled on the outside of the shipping package that it is intended for export and must bear a list of the countries to which shipment is authorized together with a statement that the drug may be sold or offered for sale only in those countries. The Committee feels this to be significant provision and directs the respective Secretaries to implement it in such a way as to assure that the required statement is legible and easily noticed. We anticipate that local enforcement personnel will be able to readily identify the destinations authorized for shipment under these amendments.

In the case of drugs to be shipped to second tier countries, the drug cannot be the subject of an action by a governmental health authority in a first tier country denying or withdrawing approval or licensing or otherwise banning the drug on the basis of safety.

Also, in the case of drugs to be exported to either second or third tier countries, the drug must be the subject of an exemption for investigational use, an application for approval or licensing, or a master file containing the safety information required for an investigational use exemption. This provision provides further assurance that hazardous drugs will not be exported. For example, if an IND exists for a human drug, under which clinical testing is being conducted in the United States, FDA is already exercising regulatory surveillance over the drug and is in a position to suspend the IND (thus automatically suspending further export to second or third tier countries), ban export, or provide relevant information to foreign countries, under appropriate circumstances.

The investigational use exemption, application for approval or licensing, or master file must cover the drug, or a drug containing the same active ingredient, thus providing that the relevant safety information will be available to the agency, and that adverse reaction reports relevant to the drug will be included. The exemption or application must remain in effect, and not be suspended, revoked, withdrawn or otherwise become inactive, to satisfy this requirement.

However, while the Committee anticipates that in the normal case a U.S. IND, INAD, NDA, or NADA will be pending when a foreign approval is granted, it recognizes that there will be cases in which for one reason or another no U.S. application has been made. Among these drugs are those identified in the proposed Section 801(e)(2)(B)(iii), directed to diseases or particular health conditions in developing countries, which do not exist to a significant extent in the United States. Because of the lack of a market in this country for drugs to treat such diseases, there is little reason for a manufacturer to submit such drugs for FDA or USDA approval. The Committee heard moving testimony that major tropical diseases, for example, still afflict millions abroad, but are virtually non-existent here. The use of a drug master file would ensure that safety data equivalent to that called for in an IND is made available to the agency and that the foreign adverse reaction reports, which would be included in the file, are also readily available. It would do this without imposing upon the manufacturer the obligation of pursuing an application in this country. The Committee notes that in its concern for the development of drugs to treat such "tropical diseases"; it has included Section 6 of the amendments,

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making it clear that such drugs are to be eligible for the development assistance and market protection contained in the Orphan Drug Act.

The notice of intent to ship required by Section 801(e)(4) to be filed with the Secretary must contain an assurance that reports of adverse drug reactions in humans will be transmitted promptly to the Secretary for inclusion in a drug master file. The Committee notes that FDA already requires adverse drug reaction reports from abroad to be included in IND and NDA files covering the drug. The Committee is very concerned that reports of serious illness or injury to persons using these drugs be made available to the appropriate personnel to permit a determination of imminent hazard to be made should the circumstance arise. However, it does not desire the needless duplication of reports. To satisfy the Committee's intent, the Secretary could require all reports covered by current regulations to go into the IND or NDA files, and reports for drugs electing instead a master file, to flow to that location, or the Secretary could require the reports to be filed in the same location as the notices required under this Act. But in either case they must promptly come to the attention of the appropriate personnel.

Section 801(e)(4) provides that the prospective exporter must furnish a notice of intent to export to the Secretary at least 90 days prior to the date of first shipment under these amendments, and the Secretary must publish this notice in the Federal Register within 15 days. Shorter time periods are provided for subsequent shipments to additional authorized countries not included in the original notice, with an additional publication requirement for shipments to other second tier countries. These Federal Register publications provide an important opportunity for broad public participation in the scrutiny of the export of such drugs. It is expected that from time to time interested individuals and organizations will furnish FDA and USDA with information not otherwise available to the agencies, which will be useful to the agency in reviewing a notice. This public process will facilitate the proper implementation and enforcement of the amendments, and will provide a convenient means by which foreign governments can remain apprised of U.S. exports under these amendments.

The Committee realizes that notifications under this amendment may, in some instances, contain confidential commercial information about drugs. The confidentiality of any such information will be governed by existing provisions regarding public disclosure under current law.

Section 801(e)(7) permits the respective Secretaries to prohibit the shipment of a drug to an authorized country upon a determination that it presents an imminent hazard to the public health in such country. Section 801(e)(8) (A) and (E) deal with the Secretary's authority to act when an importer is shipping a drug to an unauthorized country where it poses an imminent hazard. In administering such provisions the Committee intends that the phrase "imminent hazard" be interpreted consistent with its use in Section 505(e) of the FFDCA, adopted by Congress as part of the Drug Amendments of 1962.

In adopting the standard of imminent hazard, the Committee intends that implementation of this standard should comport with

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that articulated for the 1962 amendments, and cites the reasonable approach found at 21 C.F.R. § 2.5. The Committee believes that this authority should be used carefully, upon clear and convincing evidence that an imminent hazard does in fact exist. Further, while the situation needed to invoke the Secretary's authority need not rise to the level of a crisis (see *Environmental Defense Fund, Inc., v. EPA*, 465 F.2d 528, 540), the Committee intends that it must be demonstrated that there is a substantial certainty that death or serious bodily injury will result from the Secretary's failure to act under the imminent hazard authorities of paragraph (7) or (8).

The Committee is aware that while this authority has infrequently been invoked formally, it has had its effect informally and has remained a constructive and useful part of the Act. Further, because of the testing and reviewing through which modern drugs must pass before reaching the market, genuine instances of imminent hazard are few. The Committee expects that the safeguards contained in these amendments will have a similar effect, particularly the prior approval by a developed first tier country, and anticipates that the imminent hazard authority will rarely be used. Nevertheless, it remains a valuable, overriding, ultimate protection which should be used when vigorously appropriate.

Some have suggested that S. 1848 should be expanded to govern the export of antibiotics. However, the Committee feels that this is not the proper time nor the proper vehicle for the consideration of such an action.

In summation, the Committee has studied extensively the issue of the export of unapproved drugs and has heard considerable testimony from those favoring exceptions to our current law and from those opposing them. The Committee is of the opinion that there are compelling economic, competitive, safety and humanitarian reasons for revising our current policy. It finds that policy to be ineffective in protecting others. It feels that the amendments contained in S. 1848 as reported make the United States an option for the location of plants to manufacture responsible drugs not yet approved by the Food and Drug Administration or the USDA, an option which does not presently exist. They are well reasoned, carefully balanced, and offer a distinct improvement on current law.

Further, in Section 7 of S. 1848 as reported, the Committee has adopted an amendment to Section 402(d)(2) of the Federal Food, Drug and Cosmetic Act, (21 U.S.C. 342(d)(2)), having to do with confectionery. Under section 402(d)(2), confectionery is adulterated, and therefore cannot be distributed in interstate commerce if it contains liqueur or other alcohol, except for marginal amounts (0.5% or less by volume) derived solely from the use of flavoring extracts. States are free, however, to permit the marketing and sale within their own borders of chocolate and other confections containing alcohol (and not just flavoring extracts) and numerous states have done so.

Under current Federal law, confectionery that contains alcohol may not be produced in one state and sold in another, even though such goods may conform to all applicable laws of the states involved. The Committee views the current prohibition of section 402(d)(2) to be an unnecessary impediment to interstate commerce. There is no significant Federal interest in preventing the interstate

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shipment of confectionery containing alcohol between or among those states that have exercised their historic jurisdiction over alcohol and authorized such products to be sold within their borders.

The amendment adopted by the Committee would thus permit the interstate shipment of confectionery containing alcohol so long as the confectionery conforms to the laws of the state(s) in which it is intended to be offered for sale. The amendment adopted by the Committee would have no impact whatsoever on the laws of any state and would not authorize the distribution of confectionery with alcohol to states where the sale of such products is not allowed. Thus, each state will remain free to determine for itself whether and under what conditions confectionery with alcohol may be sold.

Finally, the Committee is aware that no funds are authorized to be appropriated for FY 1986 for any of the functions required under these amendments, including the expansion of DHHS or USDA staff, to implement the authority granted in Section 801(e) of the FFDCA as added by this legislation. Nevertheless, the Committee directs the respective Secretaries to take all necessary steps to implement the amendments expeditiously. Expenses incurred in FY 1986 are to be taken from existing funds.

VI. Votes in Committee

S. 1848 was brought up for markup at the Committee Executive Session on November 19, 1985. At that time two amendments were proposed by Senator Simon. One of these shortened the completion date of the first GAO study called for in the bill from three years to two years. The other was a nonrelated amendment which permits the interstate shipment of confections containing alcohol to states in which the marketing of such confections is permitted. Both amendments were adopted without objection.

Following the adoption of the Simon amendments, S. 1848 as amended was ordered reported favorably from Committee by a vote of 13-2 with one abstention as follows:

YEAS	NAYS

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YEAS	NAYS	ABSTENTION
Hatch	Metzenbaum	Weicker
Stafford	Matsunaga	
Quayle		
Nickles		
Hawkins		
Thurmond		
Wallop		
Grassley		
Kennedy		
Pell		
Dodd		
Simon		
Kerry		

VII. Cost Estimate

U.S. Congress,
Congressional Budget Office,
Washington, DC, December 17, 1985.

Hon. Orrin G. Hatch,
Chairman, Committee on Labor and Human Resources,
U.S. Senate, Washington, DC.

Dear Mr. Chairman: The Congressional Budget Office has prepared the attached cost estimate for S. 1848, the Pharmaceutical Export Act of 1985, as ordered reported by the Senate Committee on Labor and Human Resources on November 19, 1985.

If you wish further details on this estimate, we will be please to provide them.

With best wishes,
Sincerely,

Rudolph G. Penner.

CONGRESSIONAL BUDGET OFFICE COST ESTIMATE

1. Bill number: S. 1848.
2. Bill title: Pharmaceutical Export . t of 1985.
3. Bill status: As ordered reported by the Senate Committee on Labor and Human Resources on November 19, 1985.
4. Bill purpose: To amend the Federal Food, Drug and Cosmetic Act to establish conditions for the export of drugs.
5. Estimated cost to the Federal Government:

[By fiscal years, in millions of dollars]

	1986	1987	1988	1989	1990
Estimated authorization level:					
FDA		3.0	4.0	4.0	4.0
Studies		1.0	1.0	1.0	1.0
Total estimated authorization level		4.0	5.0	5.0	5.0
Estimated outlays:					
FDA		2.7	3.9	4.0	4.0
Studies		1.0	1.0	1.0	1.0
Total estimated outlays		3.7	4.9	5.0	5.0

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The costs of this bill fall within function 550.

Basis of estimate: This bill would amend the Federal Food Drug and Cosmetic Act to allow new drugs that have not been approved in the United States to be shipped to developed countries that have an adequate drug approval process, as determined by the Secretary of Health and Human Services. S. 1848 would require the Secretary to monitor the licensing and labeling status of exported new drugs, review applications to ship drugs, investigate reported violations of the bill and monitor continued compliance with the provisions of the bill. These activities would be carried out by the Food and Drug Administration (FDA).

No cost is included in this estimate for fiscal year 1986 as the bill specifically states that its provisions do not authorize the appropriation of any funds for 1986. We estimate that this bill could cost the FDA about $3 to $4 million each fiscal year thereafter. The actual cost to the Federal Government would depend on the extent to which FDA would expand to accommodate the increased workload. The bill would also require two studies. The Comptroller General would conduct an ongoing study on drug labeling and on the introduction of exported drugs into unauthorized countries. The National Academy of Sciences would report within five years on the economic impact of this bill and on the bill's effect on international health, CBO estimates the total cost of both these studies to be about $1 million in each fiscal year after 1986.

6. Estimated cost to State and local government: The budgets of state and local governments will not be affected directly by the enactment of this bill.

7. Estimate comparison: None.

8. Previous CBO estimate: None.

9. Estimate prepared by: Carmela Dyer.

10. Estimate approved by: C.G. Nuckols (for James L. Blum, Assistant Director for Budget Analysis).

VIII. Regulatory Impact Statement

The Committee has determined that there will be a net decrease in regulatory burden, coupled with an increase in paperwork, as a result of this bill. Current law prohibits the export of certain pharmaceuticals not yet approved in the United States. S. 1848 would partially remove that prohibition under controlled circumstances.

The bill will affect persons who manufacture pharmaceuticals within the United States and who, upon passage of this bill, would wish to manufacture unapproved pharmaceuticals in this country for export. The number of these persons is expected to be less than 100. The economic impact upon these pharmaceutical manufacturers is expected to be favorable, although the exact amount of increased exports can only be estimated, as described in Section II of

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this report, and the amount of increased profit from such expanded operations is unknown.

The pharmaceutical industry is a highly regulated industry. The drug approval process, from the initiation of studies through post-marketing surveillance, generates an enormous stream of paperwork. Further, pharmaceutical manufacturing facilities are required under current regulations to keep detailed records of processes, manufacturing parameters, quality control inspections, product movements and so forth. These copious records must be maintained and made available for federal review. In this context, the requirement of the bill that notification of intent to export be sent to the appropriate Secretary, that certain adverse reaction reports be included in the appropriate file, and that exporters enter into agreements with their importers relating to further export by the latter, are insignificant paperwork burdens.

Finally, the Committee notes that the paperwork burden is not imposed on current commercial activities—use of these amendments is voluntary by the manufacturer/exporter. Thus the paperwork burden is voluntarily assumed as a condition for the amendments' exemption from the current export ban.

IX. Family Fairness Statement

The Committee has determined that this bill does not have an impact on family functions.

X. Section-by-Section Analysis

Section 2 of S. 1848 sets forth Congressional findings which support the need for this legislation and which describe the purpose of the amendments.

Section 3 establishes a new Subsection 801(e) of the Federal Food, Drug and Cosmetic Act, which would permit the export from the United States of new drugs, new animal drugs, or biologicals which have not yet been approved by the Secretary of Health and Human Services or the Secretary of Agriculture, as the case may be.

Section 801(e)(1) identifies drugs subject to the amendments and states that covered pharmaceuticals are deemed violative of law unless the drug is shipped only to countries described in paragraph (e)(2) and if the pharmaceuticals meet the other requirements of the bill. It also specifies that covered pharmaceuticals complying with the requirements of the amendments shall not be considered to be misbranded, adulterated or violative of the laws or sections identified.

Subparagraph (e)(2) describes the criteria for the three categories of countries to which pharmaceuticals may be shipped under these amendments. A first tier country must have an adequate governmental health authority to approve drugs including:

1. adequate scientific review of studies relating to the safety and effectiveness of drugs;
2. assurance that labeling information is accurate and in conformance with law;
3. the ability to detect and record certain serious safety problems with the drug, including adverse drug reactions; and

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4. sufficient procedures and trained personnel to administer and enforce the policies of the agency, including the capability to remove or cause to be removed from the market problem drugs.

The second tier countries are those which have an adequate governmental health authority to assure that labeling information accurately reflects and is consistent with the labeling for the drug approved or licensed by a first tier country, and adequate to meet the third and fourth requirements for first tier countries.

The third category of countries is composed of those not included in either of the first two categories, but for which the Secretary determines, on the basis of scientific evidence including clinical investigations, that the shipment of a particular drug to each country is justified to promote the public health in that country because of diseases or health conditions there which do not exist to a significant extent in the United States. This is the so-called "tropical disease" exemption.

The Secretary is required to establish the lists of first and second tier countries within ninety days after enactment. These lists are to be periodically revised. In establishing and in revising the lists, the Secretary is to consult independent experts and is to provide reasonable opportunity for public comment.

Subsection 801(e)(3) sets forth conditions which must be met before a drug can be shipped to one of the countries authorized under (e)(2). The drug must meet the existing requirements of Section 801(d)(1)(A) through 801(d)(1)(D). The drug must not be the subject of final action by the appropriate Secretary denying, withdrawing, or suspending approval or licensing or otherwise banning the drug on the basis of safety and effectiveness. The drug must not be subject of a notice by the appropriate Secretary of a determination that is manufacture in the United States is contrary to the public health or safety in the United States. In the case of a drug to be shipped to a second tier or a third tier country, the drug or a drug containing the same active ingredient or ingredients must be the subject of (1) a current IND exemption or its equivalent for animal drugs or biologicals; (2) an application for approval or licensing; or (3) a current drug master file, containing all safety information required to be included in an investigational use exemption described under (1). In the case of a drug to be shipped to a second tier country, the drug must have been first approved or licensed by a first tier country and the labeling must accurately reflect and be consistent with the labeling for that drug approved or licensed by a first tier country. Further, that labeling must be in an appropriate language for the importing country, and the drug must not have been rejected, withdrawn or banned on the basis of safety by any first tier country. Subsection 801(e)(3) also requires that the exporter comply with the notice requirements of paragraph (4) and that the outside of the drug's shipping package be labeled: "This drug may be sold or offered for sale only in the following countries: .", including a list of countries to which shipment of the drug is authorized under the law.

Subsection 801(e)(4) sets forth the "notice of intent to ship" requirements which must be satisfied before the initial shipment of the drug. The notice must be submitted at least ninety days prior

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to first shipment of the drug to any country, and is to be followed by a publication by the appropriate Secretary of a notice in the Federal Register. This notice identifies the drug to be shipped and each country to which it will be shipped. Shorter notice periods are provided for subsequent shipment to countries not on the original list under the first notice. All such notices must identify the drug, the establishment where the drug is manufactured, each country to which the exporter will ship the drug, and, in the case of a drug exported to a second tier country, a copy of the appropriate labeling. It is also to include, to the extent not in conflict with the laws of the country to which the drug is intended for export, a written agreement from each importer that the importer will not ship the drug to an unauthorized country unless prior written consent to the contrary has been obtained from the appropriate Secretary. The importer agreement is to be renewed annually upon the next shipment, if such shipment occurs later than one year from the date of the first agreement submitted. Such notices are also to include assurances that reports of serious adverse drug reactions known to the person shipping the drug will be transmitted promptly to the Secretary for inclusion in the drug master file.

Subparagraph 801(e)(5) sets out the procedure by which the Secretary reviews each notice of intent to ship before shipment is first permitted under these amendments. If the appropriate Secretary finds a failure to comply with the requirements of these amendments, an opportunity is provided for the applicant to correct the deficiencies. If no such finding is made, shipment may proceed. If the person notified of a deficiency does not correct it within sixty days, the appropriate Secretary may issue an order prohibiting shipment.

Subparagraph 801(e)(6) sets forth the power of the appropriate Secretary to stop export anytime after the shipment of a drug becomes permitted under these amendments. It provides for a shipment to be determined unlawful because it does not comply with any requirement of paragraph (e)(3). However, it also provides that for certain correctable violations of the act, the shipper shall have an opportunity to remedy the violation prior to the issuance of an order. If the corrective action specified by the appropriate Secretary is not taken, an order may then be issued, accompanied by a statement of participants and by notification that the affected person may obtain an informal hearing with respect to the order.

Subparagraph 801(e)(7) sets forth the general imminent hazard authority of the Secretary or Secretary of Agriculture. The appropriate Secretary may prohibit the shipping of a drug to any country authorized under the bill if the drug has been determined by such Secretary to present an imminent hazard to the public health in that country. Such a determination shall not be stayed pending final action by a reviewing court.

Subparagraph 801(e)(8) gives the appropriate Secretary additional authority to control the export of yet-to-be approved drugs. If it is determined that the importer of a drug is shipping it to an unauthorized country and that such shipment presents an imminent hazard to the public health in that unauthorized country, then the Secretary shall immediately prohibit shipment to such importer, and subsequently afford the shipper an opportunity for a hearing.

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If the appropriate Secretary receives credible evidence of shipment to an unauthorized country, and, upon investigation, determines that there is a reasonable basis to believe that such shipment has occurred, then the Secretary is to notify the governments of the countries involved, and to notify the person shipping the drug from the United States. The shipper then must investigate and report to the appropriate Secretary within fourteen days any findings concerning the source and cause of any shipment of the drug to the unauthorized country.

Section 4 of S. 1848 as reported sets forth a list of fifteen developed nations which are to be included in the Secretary's list of first tier countries unless the Secretary determines that a country should not be included on the list because it does not have an adequate health authority to approve drugs.

Section 5 of the bill provides for two studies. The first is to be conducted by the Comptroller General biennially. It focuses on the extent to which drugs shipped under the authority of the amendments are introduced into unauthorized countries and the effect, if any, on the health of those countries' populations. The Comptroller General will also study the extent of compliance with the amendments' requirement that drugs shipped to second tier countries be labeled consistently with the labeling of such drugs approved or licensed by countries on the first tier list.

The second study is to be conducted through the Secretary of Health and Human Services, who is to contract with the National Academy of Sciences. This study will assess the economic impact of the amendments on employment, capital investment, and trade, and the amendments' effect on international health. This study has a completion date of five years from the date of enactment.

Section 6 clarifies the Orphan Drug Act to assure that so-called "tropical diseases" are eligible for the development assistance and market protection afforded by that act. This amendment does not, however, extend the tax benefits of the Orphan Drug Act to such diseases.

Section 7 of S. 1848 as reported contains an unrelated amendment permitting the interstate shipment of confections containing alcohol to states in which the sale of such confections is lawful.

Section 8 of the bill states that no funds are authorized to be appropriated for FY 1986 under these amendments.

XI. Changes in Existing Law

In compliance with rule XXVI paragraph 12 of the Standing Rules of the Senate, the following provides a print of the statute or the part or section thereof to be amended or replaced (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italic, existing law in which no change is proposed is shown in roman):

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FEDERAL FOOD, DRUG, AND COSMETIC ACT

CHAPTER I—SHORT TITLE

SECTION 1. This Act may be cited as the Federal Food, Drug, and Cosmetic Act.

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CHAPTER IV—FOOD

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ADULTERATED FOOD

SEC. 402. A food shall be deemed to be adulterated—

(a)(1) If it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health; or

(2)(A) if it bears or contains any added poisonous or added deleterious substance (other than one which is (i) a pesticide chemical in or on a raw agricultural commodity; (ii) a food additive; (iii) a color additive; or (iv) a new animal drug) which is unsafe within the meaning of section 406, or (B) if it is a raw agricultural commodity and it bears or contains a pesticide chemical which is unsafe within the meaning of section 408(a); or (C) if it is, or it bears or contains, any food additive which is unsafe within the meaning of section 409: *Provided,* That where a pesticide chemical has been used in or on a raw agricultural commodity in conformity with an exemption granted or a tolerance prescribed under section 408 and such raw agricultural commodity has been subjected to processing such as canning, cooking, freezing, dehydrating, or milling, the residue of such pesticide chemical remaining in or on such processed food shall, notwithstanding the provisions of sections 406 and 409, not be deemed unsafe if such residue in or on the raw agricultural commodity has been removed to the extent possible in good manufacturing practice and the concentration of such residue in the processed food when ready to eat is not greater than the tolerance prescribed for the raw agricultural commodity; or (D) if it is, or it bears or contains, a new animal drug (or conversion product thereof) which is unsafe within the meaning of section 512; or

(3) if it consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food; or (4) if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health; or (5) if it is, in whole or in part, the product of a diseased animal or of an animal which has died otherwise than by slaughter; or (6) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (7) if it has been intentionally subjected to radiation, unless the use of the radiation was in conformity with a regulation or exemption in effect pursuant to section 409.

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(b)(1) If any valuable constituent has been in whole or in part omitted or abstracted therefrom; or (2) if any substance has been substituted wholly or in part therefor; or (3) if damage or inferiority has been concealed in any manner; or (4) if any substance has been added thereto or mixed or packed therewith so as to increase its bulk or weight, or reduce its quality or strength, or make it appear better or of greater value than it is.

(c) If it is, or it bears or contains, a color additive which is unsafe within the meaning of section 706(a).

(d) If it is confectionery, and—

(1) has partially or completely imbedded therein any nonnutritive object: *Provided,* That this clause shall not apply in the case of any nonnutritive object if, in the judgement of the Secretary as provided by regulations, such object is of practical functional value to the confectionery product and would not render the product injurious or hazardous to health;

(2) bears or contains any alcohol other than alcohol not in excess of one-half of 1 per centum by volume derived solely from the use of flavoring extracts *except that this clause shall not apply to confectionery which is introduced or delivered for introduction into, or received or held for sale in, interstate commerce if the sale of such confectionery is permitted under the laws of the State in which such confectionery is intended to be offered for sale*; or

(3) bears or contains any nonnutritive substance: *Provided,* That this clause shall not apply to a safe nonnutritive substance which is in or on confectionery by reason of its use for some practical functional purpose in the manufacture, packaging, or storage of such confectionery if the use of the substance does not promote deception of the consumer or otherwise result in adulteration or misbranding in violation of any provision of this Act: *And provided further,* That the Secretary may, for the purpose of avoiding or resolving uncertainty as to the application of this clause, issue regulations allowing or prohibiting the use of particular nonnutritive substances.

(e) If it is oleomargarine or margarine or butter and any of the raw material used therein consisted in whole or in part of any filthy, putrid, or decomposed substance, or such oleomargarine or margarine or butter is otherwise unfit for food.

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CHAPTER V—DRUGS AND DEVICES

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SUBCHAPTER B—DRUGS FOR RARE DISEASES OR CONDITIONS

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DESIGNATION OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 526. (a)(1) The manufacturer or the sponsor of a drug may request the Secretary to designate the drug as a drug for a rare disease or condition. If the Secretary finds that a drug for which a

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request is submitted under this subsection is being or will be investigated for a rare disease or condition and—

(A) if an application for such drug is approved under section 505,

(B) if a certification for such drug is issued under section 507, or

(C) if a license for such drug is issued under section 351 of the Public Health Service Act, the approval, certification, or license would be for use for such disease or condition, the Secretary shall designate the drug as a drug for such disease or condition. A request for a designation of a drug under this subsection shall contain the consent of the applicant to notice being given by the Secretary under subsection (b) respecting the designation of the drug.

(2) For purposes of paragraph (1), the term "rare disease or condition" means any disease or condition *(including a disease or condition prevalent in a developing country)* which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

(b) Notice respecting the designation of a drug under subsection (a) shall be made available to the public.

(c) The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

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CHAPTER VIII—IMPORTS AND EXPORTS

SEC. 801. (a) The Secretary of the Treasury shall deliver to the Secretary of Health, Education, and Welfare, upon his request, samples of food, drugs, devices, and cosmetics which are being imported or offered for import into the United States, giving notice thereof to the owner or consignee, who may appear before the Secretary of Health, Education, and Welfare and have the right to introduce testimony. The Secretary of Health, Education, and Welfare shall furnish to the Secretary of the Treasury a list of establishments registered pursuant to subsection (i) of section 510 and shall request that if any drugs or devices manufactured, prepared, propagated, compounded, or processed in an establishment not so registered are imported or offered for import into the United States, samples of such drugs or devices be delivered to the Secretary of Health, Education, and Welfare, with notice of such delivery to the owner or consignee, who may appear before the Secretary of Health, Education, and Welfare and have the right to introduce testimony. If it appears from the examination of such samples or otherwise that (1) such article has been manufactured, processed, or packed under insanitary conditions or, in the case of a device, the methods used in, or the facilities or controls used for, the manufacture, packing, storage, or installation of the device do

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not conform to the requirements of section 520(f), or (2) such article is forbidden or restricted in sale in the country in which it was produced or from which it was exported, or (3) such article is adulterated, misbranded, or in violation of section 505, then such article shall be refused admission, except as provided in subsection (b) of this section. The Secretary of the Treasury shall cause the destruction of any such article refused admission unless such article is exported, under regulations prescribed by the Secretary of the Treasury, within ninety days of the date of notice of such refusal or within such additional time as may be permitted pursuant to such regulations. Clause (2) of the third sentence of this paragraph shall not be construed to prohibit the admission of narcotic drugs the importation of which is permitted under the Controlled Substances Import and Export Act.

(b) Pending decision as to the admission of an article being imported or offered for import, the Secretary of the Treasury may authorize delivery of such article to the owner or consignee upon the execution by him of a good and sufficient bond providing for the payment of such liquidated damages in the event of default as may be required pursuant to regulations of the Secretary of the Treasury. If it appears to the Secretary of Health, Education, and Welfare that an article included within the provisions of clause (3) of subsection (a) of this section can, by relabeling of other action, be brought into compliance with the Act or rendered other than a food, drug, device, or cosmetic, final determination as to admission of such article may be deferred and, upon filing of timely written application by the owner or consignee and the execution by him of a bond as provided in the preceding provisions of this subsection, the Secretary may, in accordance with regulations, authorize the applicant to perform such relabeling or other action specified in such authorization (including destruction or export of rejected articles or portions thereof, as may be specified in the Secretary's authorization). All such relabeling or other action pursuant to such authorization shall in accordance with regulations be under the supervision of an officer or employee of the Department of Health, Education, and Welfare designated by the Secretary, or an officer or employee of the Department of the Treasury designated by the Secretary of the Treasury.

(c) All expenses (including travel, per diem or subsistence, and salaries of officers or employees of the United States) in connection with the destruction provided for in subsection (a) of this section and the supervision of the relabeling or other action authorized under the provisions of subsection (b) of this section, the amount of such expenses to be determined in accordance with regulations, and all expenses in connection with the storage, cartage, or labor with respect to any article refused admission under subsection (a) of this section, shall be paid by the owner or consignee and, in default of such payment, shall constitute a lien against any future importations made by such owner or consignee.

(d)(1) A food, drug, device, or cosmetic intended for export shall not be deemed to be adulterated or misbranded under this Act if it—

(A) accords to the specifications of the foreign purchaser,

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(B) is not in conflict with the laws of the country to which it is intended for export,

(C) is labeled on the outside of the shipping package that it is intended for export, and

(D) is not sold or offered for sale in domestic commerce.

This paragraph does not authorize the exportation of any new animal drug, or an animal feed bearing or containing a new animal drug, which is unsafe within the meaning of section 512.

(2) Paragraph (1) does not apply to any device—

(A) which does not comply with an applicable requirement of section 514 or 515,

(B) which under section 520(g) is exempt from either such section, or

(C) which is banned device under section 516,

unless, in addition to the requirement of paragraph (1), the Secretary has determined that the exportation of the device is not contrary to public health and safety and has the approval of the country to which it is intended for export.

(e)(1)(A) A drug (including a biological product) intended for human or animal use which—

(i) requires approval by the Secretary under section 505 or section 512, or

(ii) requires licensing by the Secretary under section 351 of the Public Health Service Act or by the Secretary of Agriculture under the Act of March 4, 1913 (known as the Virus Serum Toxin Act),

before it may be shipped in interstate commerce to a country and which does not have such approval or license shall be deemed misbranded, adulterated, and in violation of such sections or Acts unless the drug is shipped by a person only to a country described in paragraph (2) and if the drug meets the requirements of subparagraph (B) and paragraph (3).

(B) If a drug (including a biological product) described in subparagraph (A) that is manufactured, processed, packaged, or held in conformity with current good manufacturing practice and that is not adulterated under subsection (a)(1), (a)(2)(A), (a)(3), (c), or (d) of section 501 is shipped by a person to a country in accordance with this subsection, such drug shall not be considered to be in violation of section 505 or 512, section 351 of the Public Health Service Act, or the Act of March 4, 1913 (known as the Virus Serum Toxin Act), and shall not be deemed to be adulterated or misbranded for purposes of this Act.

(2)(A) A drug described in paragraph (1) may be shipped to—

(i) a developed country which is on the list established by the Secretary of countries which have an adequate governmental health authority to approve drugs including—

(I) regulatory procedures to assure adequate scientific review of the animal and clinical studies relating to the safety and effectiveness of drugs before drugs are approved for marketing;

(II) regulatory procedures to assure that labeling information provided in such country to physicians, pharmacists, and patients is accurate and conforms with the laws of such country;

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(III) regulatory procedures to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

(IV) procedures and trained personnel to administer and to enforce the policies of that authority, including the capability to remove or cause to be removed from the market drugs which present a serious safety problem in such country; or

(ii) a developed country which is on the list established by the Secretary of countries which have an adequate governmental health authority—

(I) to assure that labeling information provided in such country to physicians, pharmacists, and patients accurately reflects, and is consistent with, the labeling for the drug approved or licensed by a country on the list established by the Secretary under clause (i);

(II) to detect and to record serious problems with respect to the safety of the drug, including adverse drug reactions; and

(III) which has procedures and personnel sufficient to administer and to enforce the policies of that authority, including the capability to remove or cause to be removed from the market drugs which present a serious safety problem in such country; or

(iii) a country which is not included on the list established by the Secretary under clause (i) or (ii) if the Secretary determines that, on the basis of scientific evidence including clinical investigations, the shipment of such drug to such country is justified to promote the public health in such country because of diseases (such as tropical diseases) or particular health conditions in such country which do not exist to a significant extent in the United States.

(B) Within ninety days after the date of enactment of this subsection, the Secretary shall establish the lists of countries required by clauses (i) and (ii) of subparagraph (A).

(C) The Secretary shall periodically revise the lists of countries established under clauses (i) and (ii) of subparagraph (A).

(D) In establishing and revising the lists of countries under clauses (i) and (ii) of subparagraph (A), the Secretary—

(i) shall consult with independent experts in the field of drug regulation; and

(ii) shall provide reasonable opportunity for public comment before such lists are established or revised.

(3) A drug described in paragraph (1) may be shipped by a person to a country on a list established under clause (i) or (ii) of paragraph (2)(A) or a country described in clause (iii) of such paragraph only if—

(A) the drug meets the requirements of subparagraphs (A) through (D) of subsection (d)(1);

(B) the drug is not the subject of final action by the Secretary or the Secretary of Agriculture denying, withdrawing, or suspending approval or licensing or otherwise banning the drug on the basis of safety and effectiveness;

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(C) the drug is not the subject of a notice by the Secretary or Secretary of Agriculture of a determination that the manufacture of the drug in the United States for shipment to a country is contrary to the public health and safety in the United States;

(D) in the case of a drug to be shipped to a country on the list established under clause (ii) of paragraph (2)(A) or a country described in clause (iii) of such paragraph, the drug (or a drug containing the same active ingredient or ingredients) is the subject of—

(i) a current application for exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

(ii) an application for approval or licensing as described in paragraph (1)(A); or

(iii) a current drug master file containing all safety information required to be included in an application for an exemption for investigational use from the approval or licensing requirements described in paragraph (1)(A);

(E) in the case of a drug to be shipped to a developed country on the list established under clause (ii) of paragraph (2)(A)—

(i) the drug has been approved or licensed by a country included on the list established under clause (i) of paragraph (2)(A);

(ii) the labeling of the drug accurately reflects and is consistent with the labeling for such drug approved or licensed by a country on the list established under clause (i) of paragraph (2)(A);

(iii) the labeling is in an appropriate language for the importing country; and

(iv) the drug is not the subject of an action by a governmental health authority in a country on the list established under clause (i) of paragraph (2)(A) denying or withdrawing approval or licensing or otherwise banning the drug on the basis of safety;

(F) the person seeking to ship the drug has complied with paragraph (4) with respect to such drug; and

(G) the outside of the shipping package of such drug is labeled with the following statement: 'This drug may be sold or offered for sale only in the following countries: ';
the blank space therein being filled with a list of the countries to which shipment of the drug is authorized under this subsection.

(4)(A) A person seeking to ship a drug pursuant to this subsection shall submit to the Secretary or the Secretary of Agriculture, at least ninety days prior to the date of the first shipment of the drug, a notice of intent to ship such drug. Within fifteen days after receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which identifies the drug to be shipped and states each country to which the drug will be shipped.

(B) A person who has met the requirements of this subsection with respect to a drug including the submission of a notice under subparagraph (A) and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(i), which country was not in-

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cluded in the notice submitted under subparagraph (A), shall submit to the Secretary or Secretary of Agriculture, at least fourteen days prior to the date of the first shipment of the drug to that country, a notice of intent to ship.

(C) A person who has met the requirements of this subsection with respect to a drug and who seeks to ship such drug to a country on the list established under paragraph (2)(A)(ii) for which such person has not submitted a notice under subparagraph (A) with respect to such drug shall submit to the Secretary or Secretary of Agriculture, at least thirty days prior to the date of the first shipment of the drug to that country, a notice of intent to ship. Within fifteen days of receipt of such notice of intent to ship, the Secretary or Secretary of Agriculture shall publish in the Federal Register a notice which identifies the drug to be shipped and states the country to which the drug will be shipped.

(D) Any notice of intent to ship submitted to the Secretary or Secretary of Agriculture under this paragraph shall—

(i) identify the drug to be shipped;

(ii) identify the establishment where the drug has been or will be manufactured;

(iii) identify each country to which such person will ship the drug;

(iv) in the case of a drug to be shipped to a country on the list established under paragraph (2)(A)(ii), include a copy of the labeling described in paragraph (3)(E)(ii);

(v) include, to the extent not in conflict with the laws of the country to which the drug is intended for export, a written agreement from each importer to whom the drug is to be shipped from the United States that such importer will not ship the drug to a country to which the drug may not be shipped under the requirements of paragraph (2)(A) unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture; and

(vi) include assurances that, to the extent not otherwise required under this Act, reports of serious adverse drug reactions known to the person shipping the drug from the United States shall be transmitted promptly to the Secretary for inclusion in a drug master file.

The written agreement required under clause (v) shall be renewed annually or upon the next shipment if such shipment occurs later than one year from the date of the first agreement submitted under this paragraph.

(5)(A) Within sixty days after a person submits a notice of intent to ship with respect to a drug under paragraph (4)(A), the Secretary or the Secretary of Agriculture may determine that a proposed shipment of a drug does not comply with all the requirements of paragraphs (1) through (4). If the Secretary or the Secretary of Agriculture makes such a determination, the Secretary or the Secretary of Agriculture shall, at the time of such determination, provide such person with a written statement specifying—

(i) the deficiencies which such person must correct in order to enable such shipment to comply with such requirements; and

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(ii) that such person has a reasonable opportunity to correct such deficiencies within sixty days after receiving such statement.

(B) If a person who has received a statement under subparagraph (A) does not correct the deficiencies specified in such statement within sixty days after receiving such statement, the Secretary or the Secretary of Agriculture may issue an order stating that the shipment of a drug with respect to which such statement was made does not comply with all the requirements of this subsection and prohibiting such shipment.

(6)(A) Except as provided in subparagraphs (B) and (C), at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of Agriculture may determine that such shipment is unlawful because such shipment does not comply with any requirement of paragraph (3), and may issue an order to prohibit such shipment.

(B) If, at any time after the shipment of a drug to a country is permitted under this subsection, the Secretary or the Secretary of Agriculture determines that such shipment does not comply with subparagraph (A) of paragraph (3) or subparagraphs (C) through (F) of such paragraph, the Secretary or the Secretary of Agriculture shall, prior to issuing an order with respect to such shipment under subparagraph (A) of this paragraph, provide the person who submitted the notice under paragraph (4) with respect to such shipment with a written statement which—

(i) specifies such determination; and

(ii) states that such person may, within thirty days after receiving such statement, take such action as the Secretary or the Secretary of Agriculture determines necessary to comply with the requirements of subparagraph (A), (C), (D), (E), or (F) of paragraph (3), as the case may be, in order to permit the shipment of such drug.

(C) If the Secretary or the Secretary of Agriculture determines that the person who receives a statement under subparagraph (B) does not take the action required by the Secretary or the Secretary of Agriculture under clause (ii) of such subparagraph, or that such person took an action which is inadequate to comply with the requirement of subparagraph (A), (C), (D), (E) or (F) of paragraph (3), as the case may be, the Secretary or the Secretary of Agriculture shall issue an order under subparagraph (A) with respect to such drug. Any such order shall be accompanied by a written statement—

(i) specifying each requirement of paragraph (3) which has not been complied with relating to such shipment; and

(ii) stating that the person who is the subject of such order will be provided, on request, with an opportunity for an informal hearing with respect to such order.

(7) The Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, may prohibit the shipping of a drug to a country or countries authorized under this subsection if the drug has been determined by such Secretary or officer to present an imminent hazard to the public health in such country or countries. A determination by such Secretary or officer under this paragraph shall not be stayed pending final action by a reviewing court. The authority conferred by this para-

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graph to prohibit the shipment of a drug shall not be delegated by the Secretary or the Secretary of Agriculture, except that in the case of the absence of either such Secretary, such authority may be delegated to the officer acting as such Secretary.

(8)(A) If at any time the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, determines that—

(i) a person is shipping a drug from the United States to an importer;

(ii) such importer is shipping the drug to a country to which shipment is not authorized under this subsection; and

(iii) such shipment presents an imminent hazard to public health in the country to which shipment is not authorized under this subsection,

such Secretary or officer shall immediately prohibit the shipment of the drug to such importer, give the person shipping the drug from the United States prompt notice of the determination, and afford such person an opportunity for an expedited hearing.

(B) If the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, receives credible evidence that a drug shipped to a country to which shipment is authorized under paragraph (2)(A) has been or is being shipped to a country to which shipment is not authorized under paragraph (2)(A) and if, upon investigation, such Secretary or officer determines that there is a reasonable basis to believe that such drug has been so shipped, such Secretary or officer shall immediately—

(i) notify the governments of the countries involved; and

(ii) notify any person shipping the drug from the United States of the shipment of the drug to a country to which shipment is not authorized.

(C) Any person receiving notification under subparagraph (B) shall investigate the matter and report to the Secretary or the Secretary of Agriculture within fourteen days the findings of such person, if any, regarding the source and cause of the shipment of the drug to a country to which shipment is not authorized under this subsection and the steps the person is taking to remedy any noncompliance with the terms of the importer agreement required under paragraph (1)(D)(v).

(D) If, sixty days after receiving the findings under subparagraph (C), the Secretary or the Secretary of Agriculture, or in the absence of either such Secretary, the officer acting as such Secretary, determines that despite the efforts taken under subparagraph (C), the person who imported the drug from the United States is continuing to ship the drug to a country to which shipment is not authorized under this subsection, then such Secretary or officer shall prohibit the shipping of the drug to such importer.

(E) If—

(i) a person shipping a drug from the United States has been notified under subparagraph (A) that the shipment of the drug presents an imminent hazard, and such person continues to ship such drug from the United States to a prohibited importer, or

(ii) sixty days after the Secretary receives the findings under subparagraph (C), a person continues to ship a drug from the

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United States to an importer knowing that the importer is continuing to ship the drug to a country to which shipment is not authorized,

then the drug shall be deemed to be misbranded and shall not be shipped unless prior written consent to the contrary has been obtained from the Secretary or the Secretary of Agriculture.

(F) The authority conferred by this paragraph shall not be delegated by the Secretary or the Secretary of Agriculture.

OTHER LAW AFFECTED BY THIS LEGISLATION

SECTION 5 OF THE ORPHAN DRUG ACT

GRANTS AND CONTRACTS FOR DEVELOPMENT OF DRUGS FOR RARE DISEASES AND CONDITIONS

SEC. 5. (a) The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in defraying the costs of qualified clinical testing expenses incurred in connection with the development of drugs for rare diseases and conditions.

(b) For purposes of subsection (a):

(1) The term "qualified testing" means—

(A) human clinical testing—

(i) which is carried out under an exemption for a drug for a rare disease or condition under section 505(i) of the Federal Food, Drug, and Cosmetic Act (or regulations issued under such section); and

(ii) which occurs after the date such drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 505(b) or 507 of such Act or under section 351 of the Public Health Service Act; and

(B) preclinical testing involving a drug for a rare disease or condition which occurs after the date such drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 505(b) or 507 of such Act or under section 351 of the Public Health Service Act.

(2) The term "rare disease or condition" means any disease or condition *(including any disease or condition prevalent in a developing country)* which occurs so infrequently in the United States that there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

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(c) For grants and contracts under subsection (a) there are authorized to be appropriated $4,000,000 for fiscal year 1986, $4,000,000 for fiscal year 1987, and $4,000,000 for fiscal year 1988.

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XII. Minority Views of Senator Howard M. Metzenbaum

INTRODUCTION

S. 1848, a bill which would undermine the safety of America's drug exports, is the most disturbing piece of special interest legislation passed by the Labor Committee this year. Designed to enhance the bottom line of the country's most profitable industry, the bill would in fact jeopardize the health and safety of millions of foreign consumers and Americans travelling abroad; pervert the "Made in America" label; and codify an immoral double standard in our food and drug laws.

Aside from enriching certain drug companies, this so-called "reform" legislation fails to live up to its proponents' claims. This bill will not promote world health nor will it bring new cures for tropical diseases. It is not a massive jobs bill, nor a dramatic cure-all for the trade deficit. S. 1848 will not persuade our biotechnology firms to turn their backs on their many foreign partners, nor induce U.S. firms to repatriate their overseas operations. Even if all of the proponents claims were true, they could not justify placing the safety of millions of people at risk.

Moreover the supposed safeguards in S. 1848 are only cosmetic devices to gloss over dangers inherent in this legislation.

The bill prohibits re-export of unapproved drugs to Third World countries which do not have the resources to protect their citizens from drug related hazards. Yet the FDA, which must enforce this ban, has warned that it cannot police such a restriction.

The "imminent hazard safeguard" actually precludes the FDA from acting to control an export until the damage has been done.

Another so-called safeguard requires an exportable drug to reach an early stage in the FDA approval process. Yet 90% of the drugs that clear this supposed hurdle later drop out of the approval process in the course of subsequent testing on human beings.

In reality, this bill is not about jobs, trade, or safeguards. It is, as the Philadelphia Inquirer described an earlier version of this legislation, a "greed bill."

Of course there are those who say, "every other major country exports unapproved drugs so why shouldn't we?" Since when does this great nation play "follow the leader" in questions of international morality? The conduct of other countries does not negate our obligation to ensure, to the best of our ability, that drug companies operating in the United States do not export risks and hazards to consumers abroad.

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I. S. 1848 DOES NOT LIVE UP TO ITS PROPONENTS CLAIMS

A. This bill does not promote world health

It is claimed that this bill will promote world health by halting the current practice of U.S. firms going overseas to manufacture drugs which are not approved in this country. Instead, these drugs will be manufactured in the U.S. with all the "protections" that implies.

There is no provision in S. 1848 which will prevent U.S. drug companies from continuing to locate their operations abroad. Even if the bill offered such a provision, unapproved, unscrutinized drugs made on "safe soil" are still unapproved, unscrutinized drugs. S. 1848 takes away the only real protection this country offers—approval of safety and effectiveness by our own Food and Drug Administration.

B. Tropical diseases

The proponents of S. 1848 cite its tropical disease provision as a significant contribution to world health.

Yet lifting the ban on unapproved drug exports will not aileviate the scarcity of tropical disease drugs since it is not the FDA approval process which inhibits American companies from developing and marketing tropical disease drugs.

Currently, one U.S. drug company has already applied for, and received, approval from the FDA for a drug to treat the tropical disease known as "river blindness." Two other tropical disease drugs are currently in the FDA approval pipeline and a third is expected to be submitted for testing and approval shortly.

In addition, the Office of Technology Assessment has recently published a major study on medical technology for tropical diseases. Their findings do not cite any need for a change in our drug export laws. The report instead cites the poverty of Third World countries as the major factor which inhibits American drug companies from developing tropical diseases drugs. In other words, it is not profitable to market drugs for rare diseases endemic only to impoverished regions.

The OTA report suggests a number of options including increased funding for research and getting private companies to develop medical technologies by guaranteeing purchases of products and assisting in field trials. The FDA, acting under the current "orphan drug" law, has already designated two tropical disease drugs as "orphan drugs" and is expected to designate a third shortly.

Proponents of S. 1848 are using the tropical disease issue as a screen to cover their real intent which is to evade the strict safety standards of our own FDA for drug exports.

C. Drug export legislation will not create a bonanza of new jobs in the U.S. pharmaceutical industry

Last year the drug industry claimed up to 50,000 new jobs could be created over the next few years by allowing the export of unapproved drugs. After the reliability of that estimate was discredited, the industry came back this year with a new estimate of 8,000 jobs.

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The Labor Institute of New York says the figure is actually 3,000 jobs.

Any job increase resulting from drug export legislation would very likely be only in the production area, since most companies' research, management, financial and marketing operations remain in the U.S. regardless of production locations. At the same time, pharmaceutical production is not at all labor intensive. As David B. Sharrock, President of Merrell-Dow U.S.A. told the Committee at its drug export hearings this year, it is customary for companies exporting drugs to produce only the active ingredient in bulk form in U.S. plants and then to ship the product to "finishing" plants in overseas locations at or near the market for which the drug is ultimately destined.

Clearly, S. 1848 is not a massive jobs bill. And there is more than jobs at stake with this legislation as can be gathered from the following quote from the International Chemical Workers Union which represents 5,600 members at 19 pharmaceutical plants around the country. In commenting on an earlier version of drug export legislation they said:

> Even if a few jobs would be created through this legislation, ICWU does not agree that this advantage outweighs the tremendous ethical disadvantages of the bill.

D. The American pharmaceutical industry does not need this bill to compete with foreign firms

In December 1984, the Department of Commerce released a report entitled a Competitive Assessment of the U.S. Pharmaceutical Industry. It concluded that the U.S. drug industry "overall remains highly competitive vis-a-vis foreign competitors". American companies have "performed well with respect to nearly every measure of competitiveness for which data was available."

Far from decrying supposedly restrictive regulations on the export of unapproved drugs, the Commerce Report stated:

> With respect to regulations, the U.S. drug regulatory system enjoys a worldwide reputation for the highest standards of drug efficacy and safety and helps to ensure that U.S. government approved pharmaceuticals have a favorable image abroad. Thus while the stringent U.S. drug approval process may be costly and time consuming, it also functions as a competitive advantage for the U.S. industry.

So, the American Pharmaceutical Industry should be trying to protect the quality and integrity of the "made in America" label rather than attempting to tarnish that label by lobbying for the export of unapproved drugs.

E. We should not allow the export of unapproved drugs because the FDA supposedly takes too long to approve new drugs

In February of 1985, the Secretary of HHS announced changes in the FDA approval process which she said will "dramatically speed the Federal Government's review of new drugs." The Secretary hailed these changes as the "most important in 20 years." The Sec-

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retary also said these new procedures would cut 20% off of approval time for new drugs.

So, according to the Administration, this problem has been solved. If the industry still has difficulties with the approval process, let it come forward with proposals for further change in that process instead of proposals to circumvent the FDA approval process by exporting unapproved drugs.

F. Drug export legislation will not prompt American companies to relocate existing overseas operations in the United States or to establish new operations in the United States

Proponents claim S. 1848 is "reform" legislation that will curb the practice of American drug companies locating their production facilities abroad as they currently do to circumvent the prohibition against unapproved exports. They imply that enactment will induce firms to repatriate some of their overseas facilities. These claims are wholly unfounded.

There is, obviously, no provision in S. 1848 that would prevent U.S. companies from maintaining their overseas facilities or building new ones. Indeed, since most foreign governments allow the export of unapproved drugs, particularly to the Third World, the incentive remains strong for U.S. companies to continue to operate from overseas locations.

The legislation would clearly not induce companies now operating overseas plants to relocate them in the U.S. In his testimony at the Committee's June 5 hearings, David B. Sharrock, President of Merrell Dow Pharmaceuticals U.S.A., stated:

> As foreign countries fiercely compete with the United States for capital investments and new jobs, these countries are prepared to create favorable economic incentives to secure such investments. Consequently, once a commitment to supply an active ingredient from a specific country is made, the approval of the drug in the U.S. will not bring the production of this active ingredient to our country.

For those companies seeking to establish new plants, general business considerations rather than the issue of export restrictions dictate the decision about plant location. At hearings on tax reform before the House Ways and Means Committee on July 11, 1985, Richard M. Furland, Chairman and Chief Executive Officer of Squibb said:

> Almost every country has its own version of a Food and Drug Administration, which all but forces pharmaceutical companies to do business "in-country". Exorbitant tariffs also require us to operate abroad if we are to compete for foreign markets with the large European and Japanese drug firms. In other words, if Squibb is to tap British, French, German and other European markets, it must be inside common market tariff barriers and subject to local food and drug rules.

In fact, American drug companies that sell their products in foreign markets have adopted methods of operation that rely on over-

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seas plants regardless of what U.S. export policy may be. According to Mr. Sharrock; President, Merrill-Dow:

> It is customary of multinational pharmaceutical companies to have facilities in major foreign countries where their drugs are sold, to carry out tableting, encapsulating and other operations to make finished drug dosage forms. The active ingredients, however, that go into making these finished dosage forms are typically produced at a small number of separate plants dedicated to manufacturing active ingredients of specific types. The active ingredients are then shipped to the local plants producing finished dosage forms.

G. S. 1848 will not end overseas technology transfers in the biotechnology industry

Proponents argue that the ban on export of unapproved drugs forces biotechnology companies to enter into partnerships with foreign companies to produce their drugs overseas. In reality, foreign partnerships have become an integral component of the way American biotechnology industry does business and these partnerships will continue irrespective of U.S. export restrictions.

In an extensive analysis of the biotechnology industry (Washington Post, December 17, 1984; May 19, 1985) analysts and industry spokespersons had the following to say:

> * * * for most companies, at the present stage of development, relationships between corporations that cut across national lines are beneficial to both parties. The technology transfer goes both ways.—Mr. Harvey Price, Industry Biotechnology Association.
>
> You need a Japanese partner to be successful in Japan—it's just the nature of the marketplace.—Mr. Barry Weiner, ENZO Biochem Inc.

According to the Post, Genentech's foreign partners have spent $47 million for overseas clinical tests on just one of Genentech's products alone. According to the company's vice president Thomas Kiley: "These arrangements are vital to our growth."

The overseas transfer of technology is, according to the Post series, "an inevitable part of doing business overseas" and "most companies agree that the clear short-term benefits of cooperation outweigh the fuzzy long-term risks."

Clearly, economic and research concerns far outweigh the laws regulating drug exports in determining technology transfer in the biotechnology industry.

H. Drug export legislation is not necessary to correct an oversight in the drafting of the 1938 amendments to the Food Drug and Cosmetic Act

The Pharmaceutical Manufacturers Association has stated:

> The ban prohibiting the export of new drugs not approved by the Food and Drug Administration results from a technical error made in drafting amendments to the Federal Food Drug and Cosmetic Act in 1938.

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The sponsors of S. 1848 have repeated this on many occasions implying that Congress never intended to [illegible] the export of unapproved drugs and that their legislation merely conforms the law to its original intent.

When asked to substantiate this claim, the American Law Division of the Congressional Research Service concluded the following:

> The legislative history of the 1983 recodification of the FDCA does not reveal any Congressional consideration of any legislative proposals to adopt language that could have been interpreted as authorizing the exportation of unapproved new drugs, nor does it contain any language that would permit an obvious inference that the failure to incorporate such language was due in whole or in part to an inadvertent drafting error. What is certain, however, is that over the past forty-six years Congress has interpreted the export provision as being unapplicable to unapproved new drugs and has on at least one occasion within the past decade rejected a legislative proposal to amend the export provision to allow even the conditional exportation of unapproved new drugs or unapproved new animal drugs.

II. THE SO-CALLED "SAFEGUARDS" IN S. 1848 ARE UNWORKABLE

The proponents of this bill maintain it contains a variety of safeguards which will protect foreign consumers and Americans traveling abroad as well as prevent the dumping of these unapproved drugs on the Third World where drug regulatory authorities are unable to control how drugs are marketed.

Unfortunately, these safeguards are unworkable.

A. Transshipment (re-export) of unapproved drugs will not be prevented by S. 1848

Supporters of this bill claim that unapproved U.S. drugs exported to European countries will not be re-exported or transshipped to the Third World.

Our own FDA has testified that such restrictions are illusory. In testimony before the Labor Committee on June 5, the FDA stated:

> I think that would be very difficult . . . Transshipment would be the responsibility of the country to which the first shipment is made.

Many European countries including France, England, Germany, Switzerland, etc., permit the export of unapproved drugs to the Third World. If these countries allow this practice, what interest will they have in ensuring that U.S. unapproved drugs are not re-exported?

The problem is really one of enforcement as our own FDA again made clear in its June 5, testimony:

> You include some kind of a provision of the legislation against transshipment, but I think that once the exportation is made and the product is in the foreign country you lose your ability to make the requirement stick and you lose your ability to police.

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The Pharmaceutical Manufacturers Association has stated it "agrees that it would be difficult to enforce a prohibition against the transshipment of drugs."

The GAO has documented our failure to control the re-export of computer and nuclear technology. If we can't control the re-export of such vital technology how can we hope to exert any real control over where these unapproved drugs end up?

Some proponents of S. 1848 dismiss any analogy between the transshipment of computer and nuclear technology and the re-export of unapproved drugs, since, they contend, the former occurs with the active connivance of the governments of the Soviet Union and the other Eastern Bloc nations. In fact, the analogy throws into high relief the futility of S. 1848's re-export ban. While the Soviet Union's active pursuit of Western technology facilitates such transshipments, the lure of profitable markets for unapproved drugs in the Third World would be just as effective a stimulus for the transshipment of unapproved drugs. At the same time, the failure to contain the illegal transshipment of computers and nuclear technology, when that is such a clear national security objective all but guarantees similar failure when the transshipments in question involve only unapproved drugs, goods which do not compromise our national security.

B. The loophole of "approved" countries

The bill lists 15 countries to which unapproved drugs can be exported. A second, unspecified list of countries will be drawn up by the Secretary of Health and Human Services. A drug cannot be exported to these "second tier" countries unless it has first been approved by one of the 15 "tier one" countries.

This approach allows other countries to decide our drug export standards. It is a risky business.

On October 11, 1985, the French government pulled the arthritis drug Isoxicam off the market. It was linked to five deaths and an undetermined number of injuries. The drug was not approved by the FDA for use in this country. We have our own strict standards to thank for that. However, under S. 1848, this drug could have been manufactured in the U.S. and shipped all over the world with the "Made in America" label.

England, another country on the "approved" list has pulled six drugs off the market over the last two years which it had earlier approved. These six drugs—Zelmid (zimeldine), Osmosin (slow-release indomethicin), Flosint (indeprofin), Methrazone (fepazone), Atthesin (alfadolene), and Flenac (fenclofenac)—were approved in the United Kingdom and withdrawn outright. These are drugs which have been linked to severe reactions and deaths. Osmosin was linked to 15 deaths and Flenac was linked to 15,000 adverse reactions and an undetermined number of deaths. None of these drugs were approved for use in the United States.

However, under S. 1848, these killer drugs could have been shipped all over the world with the "Made in America" lable.

C. The labeling loophole

S. 1848 merely requires that the outside of the shipping package state that the drugs are for export only. The package must also list

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the countries to which export is approved. One might call this the "Stevedores' protection provision" because stevedores are the only ones who will see this information.

Physicians and patient labeling will not inform people that these drugs are not approved for use in the U.S.A.

Drug companies could even use the "made in the U.S.A." claim as part of their advertising to delude foreign consumers into thinking that their drugs meet tough American standards.

Clearly, the most basic safeguard of consumer information is ignored by the labeling provisions of this bill.

D. The imminent hazard loophole

Under the bill, the Secretary can stop an unapproved drug from being exported if it poses an "imminent hazard" to foreign consumers. This provision is cited as a major safeguard in the bill.

The "imminent hazard" standard is the most difficult to apply. It has only been used once in 20 years to pull a drug off the market in the United States. Yet since 1971, there have been over 7,000 drug recalls in this country.

If this provision is used so rarely to recall a drug in the United States, how effective will it be in recalling a drug from a country thousands of miles away.

E. The FDA cannot enforce S. 1848

S. 1848 is supposedly a "reform" bill because it will enable our own FDA to police the marketing of unapproved drugs aboard which the agency currently does not do.

The FDA has a total of 7,099 employees. How many will be taken off their present assignments to determine whether unapproved drugs are being shipped to Belize or Djibouti for example?

How many FDA employees will be required to effectively police the world? Clearly, the FDA can only take resources from the drug approval process or from enforcement. Either way, drugs would be approved more slowly in this country or our consumers would have to make do with less protection if the FDA were ever to seriously monitor the export of unapproved drugs from this country.

In addition, the FDA Commissioner has stated the following in a written response to questions I submitted:

> I do not believe that the FDA should have the obligation to approve affirmatively the export of unapproved drugs. There is no practical (or scientific) way for us to judge the reasonableness of marketing a drug in a foreign country without a full and complete review of the available data. Moreover, it is difficult to see what our basis could be for believing that a drug could be marketed abroad when we have not yet seen data to support its marketing in the United States.

Clearly the FDA is unwilling and unable to take an active, affirmative role in policing the export of unapproved drugs.

F. The IND loophole

The bill states that an unapproved drug must have an IND(-Investigational New Drug) application to be shipped to a second tier

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country. The impression is given that this will ensure a drug is in the FDA pipeline and has been the subject of substantial testing.

Yet 90% of all drugs with IND's never go on to the next stage in the FDA approval process. The FDA itself has stated:

> Requiring that the exported drugs have an existing IND provides no assurance that the drugs in question will ever be approved in the United States. It is also true that no IND can give an absolute assurance of a drug's safety. It is understood that, for any drug, adverse reactions may appear in a large post-marketing population that do not appear during clinical trials. Therefore, while the existence of an IND under which patients are being treated with a drug clearly provides some information about the safety of the drug, the amount of information is limited. It is also important to recognize that the bulk of the data collected under an IND is seen by the FDA only when a new drug application is submitted except for severe adverse reactions that must be reported promptly to the agency. The existence of an IND only means that there have been adequate studies conducted on animals to demonstrate that the drug is reasonably safe to test in humans under carefully controlled conditions. Preliminary testing may then provide at least some information regarding the appropriateness of considering further use of the drug in humans.

Clearly the IND provision offers no real protection to foreign consumers who will in essence be the "guinea pigs" for unapproved drugs exported from this country.

G. The diplomatic nightmare created by S. 1848

The Secretary of HHS is called upon to determine which countries can receive unapproved drugs and which countries cannot. The decision is to be based on whether a country has an "adequate" drug approval authority.

The FDA has stated it would be "most uncomfortable to be put in the position of having to make difficult, if not impossible, subjective judgments on the relative quality of drug regulatory authorities of other states."

If the FDA finds the task "impossible" who could perform it? Congress? Do we have the resources, the right, or the inclination to say, in essence, "these are the countries which protect their citizens from bad drugs and these are the countries which do not?"

S. 1848 creates a diplomatic nightmare. Who is going to explain why Finland is on the list but Ireland is not? Switzerland but not Israel?

Under the bill, Congress names 15 countries. However, the Secretary reviews the list and can add or delete. The Secretary alone establishes the list of "second tier" countries. Clearly, the task is impossible whether it is performed by Congress or the Secretary.

Conclusion: S. 1848 incorporates a dangerous double standard for drug safety.

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CONCLUSION

When I asked the FDA commissioner how he would characterize the drug approval process in the United States he replied, "I would characterize the process as excellent and would not trade it for any other system."

We have strict standards in this country and S. 1848 unjustifiably revises our sound public policy of prohibiting the export of drugs which have not met those strict domestic standards.

This legislation sets up double standard-American consumers would be protected from unsafe, hazardous and ineffective drugs through the FDA approval process, while foreign consumers and Americans travelling abroad would receive inferior protection.

The message S. 1848 would send to the rest of the world is clear and unambiguous: "These drugs aren't good enough for us, but they're good enough for you."

How will this nation be judged if one of these unapproved drugs causes death and injury abroad while American citizens are protected because we only allowed the drug to be produced for export? Why should we tarnish the "Made in America" label?

S. 1848 has inspired world-wide opposition. Letters from consumer and health groups from countries such as Bangladesh, the Philippines, Belgium, India, the Netherlands, and Thailand, to name just a few, poured in to the Labor Committee pleading that we not pass this mean spirited bill. These groups are working together to promote controls on hazardous pharmaceuticals. They are urging exporting nations to follow the lead of the United States in this important policy area. A weakening of the U.S. position prohibiting the export of unapproved drugs would greatly hamper these efforts. The United Nations, the European Parliament and The Organization of American States are also working to tighten up drug exports from developed countries to developing and underdeveloped nations. The passage of S. 1848 runs counter to this international trend.

S. 1848 is not reform legislation. It doesn't even include antibiotics under its provision as is strongly recommended by experts in the field. Last year this proposal was accurately pegged a "greed bill." This year the industry is backing knocking on Congress' door. It believes that the health and safety of foreign consumers is not as important to Congress as the bottom line on the profit sheet of America's most profitable industry.

We may have the strictist standards for safety among all nations, but I don't hear anyone advocating less thorough standards for the FDA. What I do hear people saying is "let's circumvent the process for drug exports. After all, as long as we don't have to risk using the drugs, who cares?"

We are told that there are safeguards. The best safeguard is the one we have right now—if a drug is not proven safe and effective for use in the United States, don't export it.

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